SERUM IRON IN DEPRESSIVE STATES

(ENDOGENOUS DEPRESSION AND ALLIED CONDITIONS)

A CLINICAL AND EXPERIMENTAL STUDY

BY

BO R:SON KÄLLSTRÖM

ALMQVIST & WIKSELLS BOKTRYCKERI AB
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CHAPTER I

Concerning Endogenous Depression

Definition and Introduction

Since times of old, human anguish, depression, and melancholy have been problems as unfathomable as they have been of paramount interest. In religious forms they appear in such conceptions as Hell, Sin, and Punishment; in art and literature, as the dark side of life against the background of which the master creates his work and which endows creation with its fulness and profundity.

From a medical point of view the problem was actualized more positively when in 1896 Kraepelin, in accordance with the demands of the age to systematize, set up two comprehensive groups of mental disease, viz. dementia praecox and manic-depressive psychosis. The classification found "einen wohl vorbereiteten Boden", to quote Lange in his classical monograph concerning manic-depressive psychoses. Up to his time, exalted and agitated patients were classified as manics, and those depressed as melancholics. The changing of mood, "die Verstimmung", whether mania or depression, was found by Kraepelin to be a single morbid process. The two morbid states could pass over from one into the other, and even replace each other in the same patient. Initially he regarded these two groups as two different nosological entities. Dementia praecox consisted of a series of disease pictures, the common feature of which was a termination in dementia, a state of mental weakness. Manic-depressive psychosis was essentially different in its course, generally not resulting in dementia. "Melancholie", according to Kraepelin, was for a long time the designation of a pronounced depression and melancholy in middle age, involutional psychosis, but is now often used as a synonym for depression. A further study of the *symptomatology* of these two groups of diseases resulted, in 1911, in Bleuler's definition, viz. schizophrenia, a splitting of the personality, now usually employed instead of dementia praecox. Modifying his primary working-hypothesis, Kraepelin ascertained the *importance of constitution* for the formation of psychosis in his work "Die Erscheinungsformen des Irreseins" (1920). And in 1921 there appeared Kretschmer's "Körperbau und Charakter", a work whose views have come to the fore owing to their perspicuity. Kretchmer correlates schizophrenia with a schizoid constitution and a leptosome

type (tall, thin, and flattened), and manic-depressive psychosis with a syntonic constitution and a pyknic type ("barrel-shaped"). A pioneer in the analysis of the problem of constitution was Henrik Sjöbring in his works of 1913 to 1922. Sjöbring, by using his four *radicals of constitution* and employing a *statistical point of view,* further developed the cause and the basis of manic-depressive emotional reaction, "Verstimmung", as a variation and change of the primary personality, having a diminished potentiality and lowered habit-path formation. In this, the *sub-stable personality,* the formation of habit is constitutionally low, these people not being "canalized" into stable habits of activity and thus have greater emotional reaction to different stimuli.

On reviewing his earlier works and those of En Hsi Hsü and by adopting correlation computations and factor analyses, Thomas Moore, in 1944, stressed the predominance and conclusiveness of certain symptoms and symptom-complexes in manic and depressive states as well as in various types of schizophrenia. The "general factor" of specific emotional function seems to be the same as sub-stability, mostly called a cyclothymic temperament. Moore's work emphasizes the importance of symptomatology, but is also linked with constitution.

Sheldon (1940) has also contributed to the understanding of the problem of constitution by introducing the method of somato-typing, establishing three variables, viz. endomorphy (rounded fatness), mesomorphy (square muscularity and bigbonedness), and ectomorphy (a fragile linearity of build). He correlates these variables with psychic types. The quanta range from 1 to 7 in each variable, and mix with each other like Sjöbring's constitutional radicals.

Besides the questions concerning symptomatology and constitution, briefly sketched above, the discussion of *inheritance* is advanced regarding diagnostication. Luxenburger (1937–1940) confirms inheritance, denying the existence of any non-hereditary manic-depressive psychosis and establishing the percentage among children as 23.6 per cent. Slater (1938) confirms the incidence of depression to be 22.2 per cent in the case of children, and 11.5 per cent in that of parents of manic-depressive patients. The risk of inheritance is considered to be greater in the case of manic-depressive psychosis than in schizophrenia. In spite of the relatively pronounced risk of inheritance, the importance of releasing and exogenic factors is even given prominence in manic-depressive psychoses (Slater, amongst others). Mild cases, as for instance some of my material, often elude statistic appraisement in the statistics available. In addition, Slater, and others, also deal with inheritance of manic-depressive psychosis in relation to schizophrenia. In this connection there may be mentioned the relatively good social adaptation among such as have suffered from manic-depressive psychosis.

To sum up, it may be said that a multi-factor analysis is utilized

in establishing a diagnosis, whether a structural analysis *ad modum* Birnbaum or an analysis of personality according to Sjöbring is made. In praxis and in the individual case it is not possible to attain more than a *diagnosis of probability*. The further course of the malady decides the matter. This fact calls for the necessity of a prognostic investigation in dealing with psychiatric materials (cf. the original division by Kraepelin into the two larger groups of diseases). The problem is reviewed and dealt with, as to Swedish material, by Lundquist (1945) in his clinical investigation "Prognosis and Course in Manic-Depressive Psychoses". In this connection it is of interest to note that Rennie (1942) claims that 7 per cent of a material of 208 manic-depressive psychoses took a chronic course. Lundquist claims about the same percentage. Here we must always keep in mind the difficulty of making a differential diagnosis between manic-depressive psychosis and incipient schizophrenia, a fact stressed by almost all psychiatrists. In 1941 Hoch and Rachlin found that, of a material of 5,779 cases of schizophrenia, 415 patients, i.e. about 7 per cent, had been diagnosed as manic-depressive for at least the first five years.

The attitude to the problem has partly shifted during the last decade or two, possibly owing to some particular circumstances. One of these is presumably the psycho-analytic debate originating from Freud's theories and his conception of libido—a matter to be discussed with advantage in connection with affective reactions of various types and degrees and during different periods of life (cf. Hartmann, quoted by Bellak, 1952, in his monograph of manic-depressive psychosis). This "psychodynamic" view contributes to elucidating the subtle interaction in the psyche of man and the conception of psychosis, without in itself offering any direct results of scientific interest up to this day. A more obvious change was brought about by introducing the treatment with insulincoma in schizophrenia (Sakel, 1933), as well as electro-shock treatment (Cerletti, 1938) which has specifically good effects on depressions of the above type, and yields an improvement or recovery of about 75—90 per cent. The possible importance of the *point of time*, during the depression period, when ECT is administered is worth mentioning in this connection. See further Tillotson and Sulzbach (1945), as well as Morrow and King (quoted by Bellak), the two latter having also ascertained that ECT does not shorten the remission periods. Among others, Cook (1944) reviewed the effect of ECT, and Batt (1943) confirmed its positive effect, in the first attack of depression, of up to 96 per cent. In their monographs of 1946 and 1952 Kalinowsky and Hoch also discussed the problem. Whether the resistent cases are to be considered "borderline cases" is often a problem not discussed.

However, in practice and in clinical work, ECT, possibly combined with other treatments, is the treatment actually selected in depressions of the manic-depressive type. Furthermore, ECT can give an exjuvantibus-

diagnosis in some borderline cases verging on "exogenic types" and initially conceived of as being "psychogenic" due to a secondary neurotization. Finally, the shocks reveal the "endogenic nucleus" of the morbid process.

These two biological treatments have inspired biochemical research. ECT, particularly, represents a method which rapidly brings about complete remission or improvement, thus offering a practical possibility of following the biological correlative of mental recovery, "the mental health *in statu nascendi*".

As to nomenclature, instead of the appelation *manic-depressive psychosis* modern American literature has adopted the designation *affective reactions,* with the three sub-groups of *manic-depressive reaction: manic type, depressive type,* and *others,* respectively. This is a necessary simplification, considering the great number of groups more or less constructed. The borderline cases verging towards schizophrenia—always problematic—are sometimes called *schizo-affective reactions.*

At the Psychiatric Clinic of Uppsala University, where my material was collected, the expression *endogenous depression* is used to designate the group of depressions which, on the one hand, cannot be denoted as conditions of reactive, neurotic depressions, and which, on the other hand, is characterized by a group of disorders of vegetative functions and specific psychical symptoms of inhibition. In these respects, the mild depressions treated at the Clinic—a clinic mainly intended for neuroses and mild psychic disorders—principally resemble the condition termed *psychosis manico-depressiva* in its depressive form. Consequently, it cannot be overlooked that these endogenous depressions of my material constitute manic-depressive psychoses of a mild or cryptical type (see the chapter dealing with my material and the differential diagnosis). The term endogenous depression, while debatable and in fact debated at the Clinic, is expressive and relatively adequate, and cannot be misunderstood if one keeps in mind the above premises.[1] The writer, of course, does not want to deny the fact that exogenic factors may play a rôle in releasing a condition generally called manic-depressive psychosis. This psychosis has, above all in the German literature, generally been regarded as belonging to endogenic or hereditary psychosis in addition to schizophrenia, etc. (See above.)

[1] The discussion whether a reaction, *post* or *propter* a certain stimulus, inadequate or unnatural from a normal point of view (e.g. a depressive psychosis of a syntonic, more or less substable constitution released by an emotional trauma) should be considered as directly caused by this stimulus and exogenically conditioned, or whether the emphasis should be placed upon the constitutional endogenous disposition of the abnormal reaction, will, for reasons easily comprehensible, lead to unfruitful theorizing which by no means increases the lucidity of the conception. The writer adopts the term *released endogenous depression* in analogous cases. Lange calls this condition a *psychically produced melancholia.*

CHAPTER II

The Problem

The attempts at finding a biological correlative in mental diseases give rise to special difficulties for two reasons, among others:

First, the clinical demarcation of homogeneous material is, as was mentioned in the Introduction, a delicate problem.

Second, clinical laboratory findings are often uncertain or negative with regard to changes expected, possibly depending on the fact that probable deviations from what is normal cannot be registered by the method used.

On the material of endogenous depressions recorded in this work and personally examined, the writer has made a study of serum iron and certain problems connected with it.

The reason for choosing the subject and the object of investigation are the following:

(1) Endogenous depressions appear to represent a state of generally low biological activity.

(2) A study of heavy metals, primarily the behaviour of iron, is considered justified, since iron is regarded as occupying a central position in the metabolism of cells, especially in the biological processes of oxidation.

(3) Serum iron is of great importance in the intermediary metabolism of iron in the body, and although occurring in minute amounts of about 100 gamma per cent, it is determinable with great accuracy. (1 gamma per cent = 0.001 mg/100 ml.)

(4) The metabolism of iron possesses a normal diurnal rhythm reflected in the daily variation of the serum-iron level. Endogenous depressive states seem to displace, or even to lose, diurnal rhythm (loss of sleep, morning anguish, improvement in the afternoon), a condition corrected on recovery.

CHAPTER III

Concerning the Distribution and Metabolism of Iron in the Body

The chief functions of iron in the body are concerned with cellular respiration and the transport of oxygen to the tissues. The amount of iron in an adult man is about 4–5 g, and the greatest part—about 60 per cent—is contained in haemoglobin, 5–10 per cent in myoglobin, and 20–25 per cent, or possibly more, is thought to be storage iron, which is more or less available for haemoglobin synthesis. The iron of the enzymes of vital importance, such as cytochromes, catalases, and peroxidases, is less than 1 per cent, and the transport-iron of blood-plasma, clinically called serum-iron and given in gamma per cent, represents approximately 0.1 per cent of the body-iron.

The question of the distribution of iron within the organism during different periods of life is of great importance to a substance so intimately connected with biological activity. As to storage iron, a reserve to be regarded temporarily out of action when not needed, the liver, the greatest depot, contains 2–3 times as much storage iron per mg of fresh weight in normal men and women of the age of sixty and over as in those from 10–19 years of age (Schairer and Rechenberger, 1948). The increase in the various age-groups was successive, with a marked rise in middle age. There was also a difference between the two sexes in fertile age (20–40 years) with a much higher value for men than might be expected from the sexual differences of the serum iron. The percentual Fe content of the liver during fertile age was about 350 and 160 mg/10 g fresh tissue in men and women respectively, which is more than 2 : 1 and was statistically of significance.

The Occurrence of Iron in the Tissue of the Central Nervous System

The first findings of interest in this field were made by Biondi (1914) and Guizetti (1915) who ascertained the predominance of iron in certain grey masses of the adult brain of man and domestic animals. In 1922 Spatz carried out a detailed and exhaustive investigation into the prevalence of iron in certain centres of the brain, showing that in

a material of 116 brains of both sexes of the ages of 16–72 substantia nigra and globus pallidus contain most iron. Guided by the rapidity and intensity of the staining of the histochemical methods employed by him, he classified the tissues of the brain centres into four groups. Spatz also claimed a greater intensity of staining in adults. Müller (1922) found that the ganglia cells of putamen and substantia nigra, in contrast to other specific nerve cells, contained iron in a noticeable degree *(and that the cells containing melanin had no iron)*. Wuth (1923) established the parallelism between the above histochemical findings and the actual content of iron by carrying out chemical iron analyses on the cerebral tissues of different centres, and Freeman (1930) also made exhaustive histochemical as well as quantitative investigations. It is of interest to note that there is *no* iron-staining in the brain tissues of foetuses, and a moderate amount in infants. Iron first appears in the centres containing most iron. Furthermore, children up to adolescence reveal a lower intensity of staining of their brains. Strassman and others stated, in 1945, that the iron content of the brain increases in advancing age. In 1937 Tingey examined the distribution of iron in the brain quantitatively, thus confirming a successive rise of the percentual amounts of Fe during childhood. The content of total iron in the human brain was found by him to be about 20 mg/100 g of dried tissue. The distribution between the cortex and the white matter, corpus striatum and substantia nigra, histochemically investigated by him, offers an approximate conception of the relative distribution, confirming the fact that substantia nigra and pallidus contain about the same amount of Fe above 20 mg/100 g of fresh tissue, the latter being more than five times that of the cortex. The iron content of the thalamus, too, is relatively high. On account of our incomplete knowledge of the chemistry of the different fractions of tissue iron (see below) and in view of the nature of this work, the histochemical problems will not be discussed here. Of interest is the considerable amount of Fe in substantia nigra—a formation most developed in man and the higher apes and the centre of integration of the afferent impulses necessary for the performance of skilled and delicate motor-activity. The same is the case with pallidus, generally regarded as the chiefly efferent portion of the extrapyramidal striatic system, the highest centre of the old motor-system.

The Nature of Body-Iron

Haemoglobin, myoglobin, and the above specific enzymes belong to the haemo-proteins, its iron being present as the ferrous or ferric compound of the prosthetic porphyrine group.

The Storage-Iron Fraction is mobilized, when required, as below,

from different tissues. Generally, storage iron is not utilized in haemoglobin synthesis, but is made use of when the production of red cells exceeds their destruction. On the other hand, in the case of a surplus of iron and haemoglobin in the body, iron is transported to the depots and stored intracellularly in complexes of iron-protein, ferritin, and also in haemosiderin.

Ferritin was purified by Laufberger in 1937, and is an iron-protein complex. The protein of apoferritin (mol. wt. 460,000) binds iron up to 23 per cent. The cells produce apoferritin when needed. This formation seems to be a blockade and defence mechanism against too great an amount of free iron-ions. Apoferritin is to be regarded as a protective colloid stabilizing the iron-hydroxide component into a biologically utilizable and available form of iron (Granick, 1946–1951).

Haemosiderin exists in the same tissues as ferritin, being considered to represent a surplus of iron, or indicating a relative lack of apoferritin, and contains more iron and less protein. Its chemical nature, however, is not known in detail. When the protective colloid is lacking, haemosiderin will become more insoluble and stable (Finch *et al.* 1950) —compare also the increasing concentration of iron primarily in the depot organs the longer life lasts. Nevertheless, it is available to some extent as a secondary physiological form besides ferritin when the demand for iron is great. In 1949 Granick suggested that it is a polymerization product of ferritin, tallying with the conception of its being an abnormal stage of iron deposit in the cells.

Excretion and Absorption of Iron.—The elimination of iron is normally minute, being about 1 mg per day in an adult man, and 2–3 times this amount in an adult woman (menses, pregnancies), cf. McCance and Widdowson 1937, 1938, 1943, Hahn *et al.*, 1939 and others.

The loss is slight in relation to the content of iron in the food, usually being ten times as much as the physiological demand. On the other hand, only about 10 per cent of the iron of the food is supposed to be absorbed (Moore and Dubach, 1951). The greatest absorption occurs in the upper duodenum (Endicott *et al.*, 1949).

The regulation mechanism of iron absorption is not clear; the demand for iron available from the depots has been suggested to be the commanding factor. In his works of 1946–51, Granick discusses the function of ferritin in the cells of the intestinal mucosa. In 1947–52, Laurell dealt with the alterations of the transferrin level (see below) and a disturbed equilibrium of iron-ion activity. Hemmeler (1951) adduces certain points of view concerning neuro-vegetative control, which has possibly a hypothalamic centre. Hallgren (1954, experiments on rats) examines the problem in connection with protein-deficiency in food, and emphasizes the necessity of an adequate intake of protein.

Serum Iron

Serum iron, or plasma iron, holds a central position in the metabolism of iron, and can be looked upon as an indicator of the interchange of iron in the body. It is particularly available for analyses, in clinical praxis, too.

The knowledge of the existence of a non-haemoglobin-bound iron in serum dates from 1925 (Fontès and Thivolle). Further comprehensive investigations are reviewed in monographs by, for instance, Heilmeyer and Plötner (1937), Vahlquist (1941), Vannotti and Delachaux (1942 and 1949), Hemmeler (1951), and Laurell (1947 and 1952).

Because of the minute and constant "external" iron metabolism (absorption and excretion), plasma iron mainly belongs to the "internal" or intermediate iron metabolism, particularly as a link in the cycle of haemoglobin—plasma iron—haemoglobin, representing up to 75 per cent of the total serum iron interchange. The remaining 25 per cent belongs to the metabolism of myoglobin, storage iron, and so on.

The iron of plasma has been proved to be present in a non-dialyzable complex at the pH of the blood, but dissociates at an acid reaction (Barkan 1927 and 1933). Subsequent investigations by Laurell challenge the validity of this fact, claiming that a certain dissociation takes place at a pH of up to 7.

Fractionation with ammonium sulphate shows that serum iron is bound to globulin (Starkenstein and Harvalik, 1933) and to some extent also to albumin. Electrophoresis (Vahlquist, 1941) establishes that most iron wanders with the alpha- and beta-globulins, whereas little iron goes with the albumins in native serum.

In discussing a lower serum-iron value than expected after injections of 10 mg of $Fe^{++(+)}$, Waldenström (1944) deals with a "breaking effect" at a level of about 300 gamma per cent, and in 1945 Holmberg and Laurell demonstrated the capacity of normal human serum in binding iron to be about 300 gamma per cent, as was assumed by them in an iron protein complex. In 1947 Laurell and Ingelman were actually able to isolate the iron-binding protein in crystalline form—in its stable iron-saturated state—from serum, the molecular size of the protein being only slightly greater than that of albumin (mol. wt. 90,000). The iron-protein complex is of a reddish orange colour having a broad absorption maximum at 4,700 Å. In literature this iron-binding protein is termed "$beta_1$-metal-combining globulin" and "siderophilin", as well as "transferrin", the term used here.

The iron is in the ferric state, and the binding between iron and protein (see Surgenor *et al.*, 1949) is of an ionic nature. The uptake of iron from destroyed haemoglobin and body-cells occurs in the form of

free ions, whereas the mechanism of liberation from the plasma is not quite clear.

In normal conditions there is an excess of protein, the transferrin being saturated with serum iron (SI) up to about one third of its total iron-binding capacity (TIBC). The quotient SI/TIBC is called the saturation index, being normally about 33 per cent. The remaining transferrin available is termed the unsaturated iron-binding capacity (UIBC). The quotient SI/UIBC is thus approximately 0.7.

These typical values and the alterations of their mutual relationship —especially in case of iron deficiency—caused Laurell to adopt the reversible reaction Fe^{+++} + Fe-free-transferrin $\rightleftarrows$ Fe-transferrin with the corresponding equilibrium equation

$$\frac{[\text{Fe-transferrin}]}{[\text{Fe-free-transferrin}]} = K \times [Fe^{+++}]$$

as an expression of the importance of the transferrin level in the metabolism of iron ions.

Viewpoints on Serum Iron and Transferrin in Clinical Praxis

By various authors, the normal values of serum iron are indicated as being somewhere between 120–145 gamma per cent for men and 100–125 for women (see Hemmeler, 1951). Among the Swedish investigators, Vahlquist (1941) found this to be 142 ± 6 gamma per cent in men and 123 ± 4.5 gamma per cent in women, with great individual variations from a material of 100 subjects of 20–30 years of age, consisting of medical students and nurses. Without consciously assigning the withdrawal of the blood to any definite part of the day, Laurell (1947) found somewhat lower values in 100 subjects (on an average 124 and 108 gamma per cent in men and women, respectively). In a material of 50 subjects, Hagberg (1953) presents the same values as Vahlquist: 137 ± 6.3 and 123 ± 8.4, having a standard deviation of 32 and 44, respectively.

In judging individual serum-iron determinations, two factors of importance are to be noted, viz. *firstly* the fluctuation of serum iron in the same subject from one day to another, differing from about 30 gamma per cent (Heilmeyer and Plötner) up to more than 100 gamma per cent (Vahlquist and Høyer); *secondly*, the diurnal variation, which is stressed by Vahlquist (1941), and which normally represents a higher normal value in the morning and a drop of approximately 20–60 gamma per cent (*c.* 30 per cent) at about 6 p.m. (Høyer and Hemmeler). Hamilton *et al.* (1950) assumed the lowest value to be during periods of greatest activity. Høyer established the fact that, in

15 of 20 cases, the lowest value appeared at about midnight. Hemmeler, too, claims it to occur "parfoi vers 21 heures ou même à 23 heures, après une ou deux heures de sommeil". He also maintains the influence of sleep. The high value of serum iron in the morning depends on a sleep that is calm and sufficiently long, whereas short and unrestful sleep results in a low morning value. Furthermore, in accordance with Høyer, he confirms the fact that those working on shifts at night have a reversed and less pronounced diurnal rhythm and their highest serum-iron value in the evening, the lowest being in the morning. In 1951, Jacot found an increase of serum iron after fasting: the influence of starvation.

Serum iron decreases with the advance of age (in contrast to storage iron). In one hundred normal subjects of 20–30 years of age, Høyer found average values of 129 and 113 gamma per cent in men and women, respectively, with a standard deviation, from the mean, of about 30. In one hundred elderly subjects of 59–93 years of age, 50 men and 50 women, the serum-iron values were 110 and 104 gamma per cent respectively, with a standard deviation of about 25. The criteria of the material were sufficient, and there was a drop of statistical significance in the two groups of male individuals, *also proving an equalization in advanced age of the higher male serum-iron value manifesting itself in puberty.*

The influence of age on serum iron, also studied by Pirrie in 1952, confirms "a highly significant decrease" with advancing age in a material of 108 males and 98 females of up to 80 years. The highest values were observed during the reproductive period of life (20–40 years)—"*the period during which the activity of endocrinal factors is also at its maximum*". The values for men in the age group 21–30 years were 132 gamma per cent, and only 96 gamma per cent as early as in the age group 41–50 years. In women the values were 116 and 89 gamma per cent, respectively. This distribution of age is not sufficiently taken into account in estimating clinical material in literature. The observed sex difference was maximal during the reproductive period of life.

Actual values of the TIBC of healthy adults found by various authors and reviewed by Hagberg in 1953, range from 300–360 gamma per cent. His own investigation of 54 subjects of both sexes gave the value of 330 ± 4.9 having a standard deviation of 36. The TIBC is more stable and does not seem to possess any noticeable diurnal variation (Laurell, 1947, 1952, and others). The clinical conditions regarding iron balance and its disturbances are schematically divided into four groups:

(1) Normal conditions resulting in a normal saturation index (33 per cent).

(2) Conditions, principally in diseases of the blood, producing haemolysis or the incapacity of forming new blood, as for instance hypoplastic

and dysplastic anaemias causing an increase of SI and a decrease of TIBC as well as a high saturation index.

(3) Pure iron deficiency and an intact (or increased) protein synthesis such as in pregnancy and post-haemorrhagic states, resulting in a low SI, high TIBC, and a low saturation index.

(4) Mixed conditions of a composite nature bringing about a disturbed protein synthesis as well as an abnormal iron metabolism, as in the case of intoxications, infections, and malign tumours, resulting in a varying interrelation of the two factors.

CHAPTER IV

Earlier Investigations into the Iron Metabolism and Red-Blood Picture of Mental Diseases

The research of main interest concerning the metabolism of iron in mental disorders deals with the *tissue iron* of the central nervous system, *CSF-iron*, and *serum iron*.

In studying, histochemically as well as quantitatively, the brains from 50 patients with mental disorders (the cortex of the right frontal lobe), Freeman (1930) found a deficiency of iron in the cortical ganglion cells in schizophrenia, more pronounced in the group of 14 "schizoid psychoses" than in that of 21 "paranoid cases". Unfortunately, the material is contaminated by the somatic diseases (i.e. pulmonary tuberculosis, neoplasms) occurring simultaneously, which deprive the quantitative results of their value. Also Tchalissoff and collaborators (1936) indicate a low total content of iron in the tissue of the central nervous system in the case of schizophrenia.

By studying "haemosiderin and tissue iron" of the brain—especially in the basal ganglions of 48 patients, the part of his material not preceded by haemorrhage—Strassmann (1945) states: "Large amounts of tissue iron were often seen in globus pallidus in patients over forty years of age suffering from various types of psychosis." Strassmann assumes this increase to be "probably caused by an involutional process, after the fortieth year". Moreover, he says, "Nearly all our patients over sixty years showed a considerable amount of iron in the areas mentioned" (globus pallidus and substantia nigra, Group I of Spatz; corpus striatum and dentate nucleus, Group II of Spatz). "The largest amount of iron was seen in a woman aged 82 with signs of advanced arteriosclerosis in all the organs, including the brain. In no other case were there so many blood vessels incrustated with iron salts, nor did so many ganglion cells contain iron in the areas of Groups I and II of Spatz. On the other hand, the oldest patient who suffered from a senile psychosis and who died at the age of ninety-two showed no larger amounts of iron than were found in schizophrenics who died at the age of forty-eight."[1]

Beck (1939) found low iron values in the *spinal fluid* of schizo-

[1] The well-known fact that there is a pronounced increase of tissue iron of the brain in cases of general paralysis may be parenthetically referred to in this connection.

phrenic patients (30 years and less), which amounted to about half the normal value, viz. 24 gamma per cent.

In 30 schizophrenics Buscaino (1946) found CSF-iron to be within normal limits, i.e. 37 gamma per cent, the normal value being 34. On the other hand, he noticed an increase amounting to 55 gamma per cent in a subgroup of 13 acute catatonics of the age of 19 to 37 during the first half year of their illness. The values remained high during the entire first year. Non-catatonics of the same age groups did not show any increase.

In their investigations of 1951 on a material of 98 psychoses Lehmann and Kral observed a statistically significant decrease of liquor iron in patients having acute schizophrenia in relation to those having a chronic type as well as in relation to individuals suffering from organic psychoses, and they drew the following conclusion: "It is assumed that a low iron content of the spinal fluid is indicative of increased brain metabolism and that high iron values of the spinal fluid may reflect reduced cellular activity of the brain tissue." In 1952, on injecting iron intravenously, 100 mg of "Feojectin" (containing saccharated iron oxide in a 2 per cent solution), the authors were able, in spite of a relatively moderate increase of the serum-iron level in the few cases below 150 gamma per cent tested at the same time, to indicate an increase of CSF-iron of between 100–600 per cent of one third of the cases. This increase of CSF-iron occurred within 30 minutes. Six hours subsequent to the injection, eleven patients of eighteen revealed a significant increase. In this group, all the cases which had shown a momentary increase within thirty minutes made their appearance again. Unfortunately we do not possess any idea whatsoever of the serum-iron level of most cases nor its rise, for only three were tested together.

Concerning the *relation between serum iron and CSF-iron,* Tramontana (1948) made simultaneous tests on 20 healthy individuals. He found that, in normal conditions, the iron of CSF amounts to approximately one third of the serum iron. There was no exact correspondence between the respective values, their relationship being assumed to be regulated by complex biological functions. The above authors discuss the function of the blood-liquor barrier, in accordance with Katzenelbogen (1935).

As to *serum iron,* Heilmeyer, Keiderling, and Stüwe (1941) indicate normal, or possibly slightly increased, values in a few cases of schizophrenia. On examining four patients, Buscaino (1946) found approximately normal values in two cases of catatonia, high in one, and finally very low in the other of a dementia praecoxissima type. In 1948 Ferroni and Lipani further determined serum iron, also administering intravenous iron to each of 24 cases of schizophrenia. There were 11 chronic and 13 acute schizophrenics. The first group had received no treatment,

whereas the acute cases had. The chronic cases had a serum-iron level within normal limits (122 gamma per cent). The acute ones had a low serum-iron value (80 gamma per cent), 4 hebephrenic and 4 catatonic cases having 59 gamma per cent respectively, while five paranoid cases possessed a serum-iron level of 113 gamma per cent. The patients were given c. 7 mg of $Fe^{++(+)}$ intravenously. Those that were acute had a lower load curve, and the chronic cases a higher and a more sluggish one than what is normal with respect to the different types of iron. In conclusion, the authors discuss the incapacity of the chronic cases to make use of iron, possibly owing to a toxic blockade of the reticulo-endothelial system, a neurovegetative sluggishness or diminishing of oxidative processes, in contrast to the "voraciousness" for iron in defending the organism in acute cases of schizophrenia. The above subgroups are, as is to be seen, very small, and this work is without any possible statistical adaptation whatsoever, thus lacking universal applicability.

In 1947 Ferroni and Indovina examined the *effect of the el-shock and electro-absence on the serum-iron level.* On a material of 24 patients having various psychic maladies—in all given 28 shocks and 7 electro-absences—the authors examined the serum iron immediately prior to the shock (absence), 5 min. after, and 1 hour subsequent to the treatment. Most frequently the authors registered a drop in relation to the original value. In 18 and 20 patients, respectively, there was a decrease of the serum iron. Any idea as to the diurnal rhythm of the serum iron of the patients before the ECT was not obtained, nor was the time of the day recorded when the shocks were administered. The changes of the serum-iron level, even 5 minutes after the shock, however, were relatively great, the lowest drop being 83 gamma per cent, and the highest rise 64. The authors interpret the results as a criterion of the influence of el-shock on the serum-iron level, indicating, in this connection, a neuro-vegetative regulation of serum iron.

In 1951 Källström, dealing with a material of 20 depressed patients having endogenous depressions (collected in 1949–1951), found, independent of the investigations by Ferroni and his associates, a decrease of the serum-iron level on the recovery of the patients. Postulating that mental depression, primarily of an endogenous type, is a state of generally reduced biological activity, and taking into consideration the rhythmic variation of serum iron during the day and the central position of iron in biocatalytic processes, he found that serum iron diminished, the difference being 45 ± 6 gamma per cent, or, on recovery, approximately a drop of one third of the original value, i.e. during the time of illness.

The material was mixed, consisting of 7 men and 13 women. All of them were treated with shocks. The serum iron decreased in 19 of the 20 patients, and remained the same in one. The patients were

somatically healthy, having normal blood values and a normal SR. The distribution of age was: 14 patients belonging to the age group 35–50, 5 over 50 years, and one under 30. The period of control tests after the ECT restoring their health occurred during 1–16 days subsequent to the treatment.

The author indicates the possibility of an increased erythropoiesis as a cause contributing to the decrease of serum iron. Also, reference is made to a possible interaction of ACTH provoked by the shock.

As to the erythrocytes and erythropoiesis of mental disorders, principally in depressions, several investigations have been made that do not yield univocal results of significance. Reviewing the literature in this field, Sondén (1927), on carefully examining 11 manic-depressive psychoses continuously during the course of several years and in various ways, did not arrive at any significant variations as to erythrocytes. Two of his patients revealed slight changes of the erythrocyte number during their diseased and quiet periods, and three cases manifested a high erythrocyte number during depression (or mania), which was found to decrease in the course of their improvement during at least one of their periods.

In a critical survey of the literature, Wilder (1934) came to the conclusion that uniform changes of the peripheral blood picture cannot be found in psychic diseases. Aleksandrowicz and Marie Spiss (1947) found normal conditions of the blood-picture and of the bone-marrow in depressions of a manic depressive type. In maniacs, on the contrary, they discovered a noticeable increase of the nucleated bone-marrow cells.

As to the relation between disturbances in the central nervous system and variations of the peripheral blood picture, clinical findings are not conclusive. However, there seems to be a certain reliability concerning a possible relationship between disturbances of the central nervous system and *polyglobulia* (Guillain and collaborators, in one case of diabetes insipidus and another of diabetes and adiposogenitalis, 1931; Salus, 1933, in one case of sarcoma of the left frontal lobe; Meiner, 1936, in one of glioblastoma in the cerebrum, polyglobulia being normalized after operation; and, finally, Carpenter and associates found a normalization of the erythrocytes after removing subtentorial neoplasms in two cases). On the other hand, Lucia and Marasse (1944) could not find any relation between the haemotopoiesis and neoplasms in the pituitary and diencephalon regions in 12 cases of a material of 59 autopsies relating to patients having various affections of the brain. Günther (1929), among others, stressed the fact that narcolepsia is regarded as accompanied by high erythrocyte values, launching the term "cerebral polyglobulia".

As for the examination of the *red-blood picture in mental disorders in relation to el-shocks,* no results of any outstanding interest have been arrived at.

Felici (1940), Delay and co-workers (1943), in dealing with "le syndrome humoral du post-électro-choc", found no noticeable changes.

Hortling (1947) found a slightly varying tendency of the erythro-

cyte number as well as that of the value of haemoglobin on examining 15 patients suffering from various mental disorders while treating them with 32 el-shocks, ten being abortive. Only two of the patients were diagnosed as having a manic-depressive psychosis, seven were schizophrenic, three psychopathic, two were regarded as having psychogenic reactions, and one a presenile psychosis. Hortling's thorough investigations were primarily a study of the effect of shock on haematopoiesis. In this mixed material he could not find any obvious changes of either erythrocytes, reticulocytes, or erythrocytic nucleated bone-marrow cells.

Investigations by Parsons and co-workers (1949), among others, indicate a transient increase of the haemoglobin value immediately subsequent to shock, as Delmas-Marsalet had earlier (1946) claimed an increase of erythrocytes occasionally after shock.

Centini and Bandettini di Poggio (1939) claim a decrease of the number of erythrocytes from the fourth shock on. Hut (1948) and Bornschein and Auerswald (1949) also deal with haemodynamic problems in investigations of erythrocytes in connection with ECT.

Certain other problems of interest concerning research into mental depressions and bordering conditions are referred to in the chapter dealing with the discussion of the results.

CHAPTER V

Methods

A. Laboratory Methods

My methods deal with the determination of serum iron, the iron-binding capacity of serum, the reticulocyte counts, the determination of the volume of blood-plasma, that of the haematocrits, the serum-protein determination according to the Cu-sulphate method of van Slyke, and, finally, that of the haemoglobin and the erythrocytes.

1. *The determination of the serum iron*

The method employed goes back to that of Heilmeyer and Plötner (1937), which was modified by Vahlquist in 1941 and formed as a micromethod, used by Hagberg in 1953. *The principle* is as follows: Hydrochloric acid liberates the protein-bound serum iron. Subsequent to precipitating the protein with trichloracetic acid, the subnatant iron solution, after being centrifuged, is adjusted to a suitable pH. The actual ferric iron is transformed into ferrous iron by means of hydroquinone as a reducing agent. The iron is then spectrophotometrically determined after adding ortho-phenanthroline hydrochloride, with which it forms a red-coloured complex.

In the technical procedure the greatest care is essential with regard to the absence of contaminating iron. All the glassware was cleaned with potassium dichromate in concentrated sulphuric acid and afterwards repeatedly washed in water free of iron. Distilled water passed through a cation-exchange column was used in analysing as well as in cleaning the utensils. The centrifugation was however made in open tubes. In the analysis 6 M hydrochloric acid (pro analysi), 20 per cent trichloracetic acid (pro an.), concentrated ammonia (pro an.), M/2 hydrochloric acid, 1 per cent *p*-nitrophenol, 2 per cent hydroquinone, and 1 per cent *o*-phenanthroline hydrochloride were used.

The analytical procedure.—Serum of 0.3 ml was diluted with the same volume of water and shaken together with 0.3 ml of 6 M hydrochloric acid. After approximately 15 minutes 0.6 ml of trichloracetic acid was added. After being shaken, the mixture thus containing serum of 20 per cent was allowed to stand for 20 minutes and then centrifuged. After the protein had settled at the bottom, the iron solution was sucked up by means of a Pasteur pipette, and 1 ml was used for the analysis. The mixture was neutralized with concentrated ammonia by using one drop of *p*-nitrophenol as an indicator until the yellow colour appeared, and then adjusted accurately by M/2 hydrochloric acid. A surplus of 0.03 ml of the acid was added after the yellow tinge had just vanished. At this pH one drop of *o*-phenanthroline hydrochloride yields a red colour after reducing the iron with

one drop of hydroquinone. The extinction value was read against water in a Pulfrich photometer in microcuvettes of a length of 50 mm and with filter S 50. (The reading with filter S 50 was completed by reading with a red filter, S 66. This arrangement was carried through in accordance with the original method by Vahlquist in order to obtain a control of the absence of opalescence in the solution of the reagent.) The iron-free water utilized here—and as a diluent in the analyses—was not allowed to have a higher content of iron than 25 gamma per cent, its lowest value being 9 gamma per cent.

The calculation of the amount of iron in the samples was carried out in the following way:

$$(C_s \times V_s - C_b \times V_b) \times 2{,}500 = \text{Fe gamma per cent.}$$

V_s = final volume of the solution of *o*-phenanthroline.

V_b = final volume of the blind.

C_s = the extinction-coefficient of solution V_s calculated up to a layer-thickness of 1 cm.

C_b = the corresponding extinction-coefficient of solution V_b.

2,500 is the product of the absorbancy constant of *o*-phenanthroline-iron (5.0) and the re-calculation factor of 0.2 ml of serum up to 100 ml (500).

Accuracy of the method.—All the values given in this investigation are obtained from duplicate determinations. The standard error of 100 duplicate determinations was found to be $\sigma_m = 7.9$ ($M = 143$). When a duplicate determination of each value is made, the error of measurement will be approximately $\frac{7.9}{\sqrt{2}} = 5.6$. The error was thus about ± 4 per cent.[1]

2. *The determination of the total iron-binding capacity of serum*

The method used was that of Schade and Caroline as modified by Rath and Finch (1949).

The principle.—Ferrous iron forms a salmon-red colour in an iron beta$_1$-globulin complex on adding serum, giving a change in the serum-colour from yellow, or yellow-green, to yellow-red. The colour increases until the beta$_1$-globulin is saturated. The total amount of iron-binding globulin, i.e. the total iron-binding capacity, is obtained by a summation of the serum-iron value and the surplus of globulin titrated by adding iron up to the saturation limit. The determination is carried out spectrophotometrically (as below).

As to *the titration,* a standard iron solution containing 20 gamma of ferrous iron per ml was used. This solution was prepared by solving 14 mg of ferrous ammonium sulphate in 100 ml of iron-free water

[1] The formula $\sigma_m = \sqrt{\frac{\Sigma d^2}{2n}}$ was applied (Dahlberg 1940). The term d is the difference between the two values obtained for the same sample, n the number of differences, and σ_m the error. M denotes the mean value.

acidified by 0.5 ml of 1 M acetic acid. In addition, physiological saline was required.

The procedure of the method.—The amount of serum necessary is 2 ml. (The blood samples—vein-punctures, 5–7 ml, including blood for the serum-iron analyses—were taken at 8–9 a.m. from fasting patients.) Coleman's spectrophotometer, Model 14 having cuvettes No. 14–307, was utilized, and the readings were made at a wave-length of 5,200 Å. The total volume required was obtained by adding 3 ml of saline to the 2 ml of serum. The blank of the parallel cuvette consisted of 5 ml of saline. The transmission of this cuvette was corrected to 100 per cent. A measurement was made of the transmission of the serum dilution several times after approximately ten minutes, and was used as the basic value. The titration of the surplus of iron-binding globulin was carried out by adding 0.05 ml of the iron standard successively. The contents of the cuvette were well mixed after each portion added, and several readings were made, during at least two minutes every time. The blank-correction was performed in succession. When no further intensity of colour developed, i.e. when there was no more decrease of the transmission and when the latter remained constant, the transmission value was read another three times. The difference of the transmission was counted in per cent of the basic value. The value was obtained graphically by plotting the difference of transmission in per cent on the y-axis and the added iron expressed in gamma per cent on the x-axis, the difference being, within the range employed, a linear function of the iron added (up to the saturation limit); see Fig. 1. Above the iron-binding capacity the line runs parallel with the x-axis. The amount of iron added—the UIBC—is indicated by the point of intersection. On adding the serum value separately determined, the TIBC is obtained as a summation value. In using the method, it is necessary to observe that the standard, as an iron solution, is unstable. This fact was taken into consideration, and the solution was renewed frequently.

The samples were preserved in a refrigerator at —16° C for a period of up to three months. Duplicate determinations of up to 6–8 months yielded no significant differences in relation to values of fresh serum. Similarly, ten determinations of the same sera after one or two freezings and meltings, respectively, agreed well with each other. Tests were made on each 100 Å between 4,500 Å and 5,500 Å, covering the broad absorption band between 4,600 Å and 5,300 Å. The samples were read at 5,200 Å.

The accuracy of the method.—The standard error of 80 duplicate determinations was found to be $\sigma_m = 10.7$ ($M = 217$), the error thus being about $\pm$ 5 per cent. The absolute error being practically constant at all levels of the UIBC, the method is more reliable in the case of

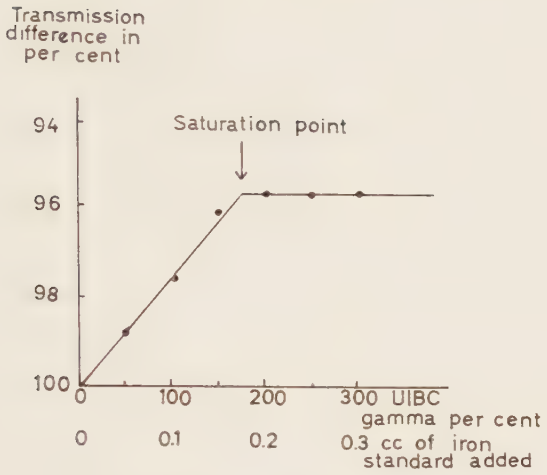

Fig. 1. A typical iron titration curve.

higher values. In my material there occurred no values below 100 gamma per cent.

The weak points of the method.—The method is practicable except in cases of lipaemic serum, severe disturbances of plasma protein, and highly discoloured serum. A bilirubinaemia of about 3 to 4 mg per cent presents too low values, but an amount of 1.0 mg per cent does not interfere with the determinations (Smith *et al.*, quoted by Hagberg). The sera included in my material were in doubtful cases tested, and were not accepted unless they had normal values with regard to the "clinical" functions of the liver (bilirubin, Hanger, thymol).

3. *Counting the reticulocytes*

The method introduced by Brecher and Schneiderman (1950) was employed. As a rule, venal blood was used, and only in a few cases capillary blood, the duplicate determinations revealing no significant differences in the various blood samplings as to the reticulocyte counts. The staining method was that of vital staining with brilliant cresyl blue as a two per cent solution in normal saline. The time of staining was 20–30 minutes, the sample being mixed thoroughly. Dry preparations were used. Nizet has shown that reticulocytes are uniformly spread among the red corpuscles in dry smears. The latter were examined through an oil-immersion objective. The 10×-ocular, having a Miller disc inserted, was applied. The reticulocytes were counted in the large

square (8/9 of the surface), and the red cells in the small one (1/9 of the surface). Twenty squares were examined, and the percentage of reticulocytes was found to be the following:

$$\frac{100 \times \text{reticulocytes in large squares}}{\text{red cells in small squares} \times 9}.$$

By this method it was only necessary to count about 200 red cells (in all the 20 fields together) and a number of reticulocytes. The standard error of Miller's technique is less than that of the standard method, in the case of lower reticulocyte counts, and up to 10 per cent of the latter (see further Brecher and Schneiderman). As a rule, my material contains rather low values. A hundred duplicate determinations present $\sigma_m = 0.36$.

4. *The determination of the plasma volume*

The Evans blue dye method, in the form applied by von Porat, was adopted. The principles of the method are discussed by von Porat in his work of 1951. As to the time of mixing and the disappearance rate, it was considered appropriate, in accordance with von Porat, to use an interval of 15 minutes between the time of injecting the dye and that of taking the sample. Poor circulation and cardiac incompensation lengthen the time of mixing. A reduced plasma protein, as in cases of serious malnutrition, increases the disappearance rate. Such factors are not regarded as obviously affecting my material.

Dissolved in serum, EB yields an absorption maximum at a wavelength of 6,200 Å, the absorption of the dye following Lambert-Beer's law. Coleman's spectrophotometer of the above type was utilized in the experiments by using 10 mm cuvette-layers. The dye was obtained from Eneqvist Holme & Co., Ltd., Stockholm, and the dye solutions were kindly produced and tested as to their toxicity by Pharmacia Ltd., Uppsala. The EB-solution of 0.3 per cent was brought about by normal saline and distributed in ampules of 5 ml. No instability was noticed by me in the solution for 1 $^1/_2$ years, this being in agreement with von Porat. The solution was standardized in the following manner: 2 ml of dye solution from an ampule was pipetted into a 50 ml flask, subsequently filled with human serum. The contents were carefully mixed, and 2 ml were diluted in the same way, the final solution thus amounting to 1: 625. By diluting the serum of the same origin to the same extent, the blank was obtained (in so doing, less amounts were needed: 4.8 + 0.2 ml, mixing and diluting 0.2 ml of the contents with 4.8 ml of the serum).

The disturbing influence of the haemolysis, amongst others discussed by Gibson and Evans (1937) and also examined by von Porat, has

only a slight influence on the wave-length of 6,200 Å. My sera did not show any noticeable haemolyses according to the duplicate determinations at a wave-length of 5,740–5,780 Å, where the effect of the haemolysis is manifested. (The haemolytic experiments revealed a pronounced absorbancy in this band.)

The technical procedure when injecting the dye.—The dye-solution was taken from an ampule to fill a 5 ml syringe, which together with its needle was then weighed with an accuracy of 1 mg. A serum blank from the patient (10 ml of blood) was taken from the cubital vein of one arm. The patients remained in bed fasting, the venal punctures being made between 8.30 and 9.30 a.m. The dye, i.e. about 15 mg, was injected into a (another) cubital vein of the same arm, and the injections were made during a period of 30 seconds. After 15 minutes a blood sample was taken from a cubital vein of the other arm. The syringe was weighed immediately after the injection so as to obtain the amount of dye injected. The volume of dye-solution injected is given by dividing the weight obtained by the specific gravity previously determined from another portion of the solution.

The blood samples from the patients were centrifuged after letting the sample coagulate (1,500 revolutions during 10 minutes).

The absorbancy of the dyed samples were recorded in a Coleman spectrophotometer at wave-lengths of 6,200 Å (and 5,780 Å) in the 10 mm layer. The sample from the patient was used as the blank before the dye was injected. The calculation of the plasma volume (PV) was obtained by comparing the value acquired with that of the standard solution known by putting the sign of equality between the absolute amounts of dye, as below:

$$V \times A_c \times S = \mathrm{PV} \times A_q, \text{ or}$$

$$\mathrm{PV} = \frac{V \times A_c \times S}{A_q},$$

V = $\frac{\text{the weight of the EB-solution}}{\text{the spec. gravity of EB-solution}}$ = vol. (ml) of dye injected,

A_c = the absorbancy obtained on standardizing the EB-solution,

S = 625 (dilution factor of the EB standard),

A_q = the absorbancy value of the patient's serum (after 15 minutes).

According to von Porat (1951), who carried out very detailed investigations of this method under standard conditions, the plasma volume of men is 3,450 ml, or 46.6 ml/kg of body-weight, and in the case of women 2,695 ml, or 44.9 ml/kg. The corresponding total blood-volume values determined by the haematocrit counts amount to 6,166 ml or 83.3 ml/kg of body weight in men, and 4,477 and 74.7 respectively

in women. As a corrective factor of the haematocrit values, 0.95 was used.[1]

The error of the method of plasma-volume determination is, according to von Porat and in agreement with earlier writers, approximately ± 5 per cent, having been determined in rabbits as well as in human beings. Owing to the importance of the method in relation to my investigations, no special control was made by me in this matter, the above error being accepted as applicable.

5. *The determination of the haematocrit values*

Von Porat's haematocrit method of 1948 was applied. A capillary tube 100 mm in length was used, inserted between two rubber packings in a metal casing. The readings were carried out with an accuracy of 0.5 mm. Duplicate determinations were made. The blood (venal punctures) was taken from a small Ellermann tube (containing dried heparin) and carefully mixed. The glass capillaries were centrifuged in the Corda centrifuge at the rate of 3,000 revolutions during a period of 30 minutes. The error of the haematocrit method was ascertained by means of 50 duplicate determinations: $\sigma_m = 0.22$. When duplicate determinations are made, the error of measurement will be $\frac{0.22}{\sqrt{2}} = 0.16$, $M = 42.58$, the error thus being below ± 0.5 per cent. The above corrective factor 0.95 was used.

6. *Other methods employed*

In order to determine the specific gravity of the serum, van Slyke's copper sulphate method was employed.

Autenrieth-Königsberger's haemometer, standardized by Enghoff at the Institute of Physiology, was utilized in determining the haemoglobin values.

The erythrocytes were counted in accordance with the method of Ellermann. Duplicate determinations were made throughout the investigation.

B. Statistical Methods

Common methods of statistics are here used (Dahlberg 1940). As to the statistical analysis of the material, the State Institute of Race Biology of Uppsala was consulted.

[1] *The total blood volume* (TBV), determined from the PV obtained by means of the hematocrit value according to the formula $TBV = \frac{PV \times 100}{100 - HCT}$, is based upon the assumption that the distribution between the cells and plasma is the same in the entire vascular system, an assumption which is, however, considered to give false values.

Concerning the criteria of significance, the difference between two means is considered statistically significant when it amounts to at least 3 times the standard error, and statistically probable when it is between 2.5 and 3 times the standard error.

With regard to successive shocks in man, the statistical method was used which has been elaborated by Fisher (1936) and Gosset. This was considered applicable owing to the small number of patients in each group. An estimation of the significance of a difference was arrived at by considering the ratio of the difference to the standard error, *t*, and the number of degrees of freedom. P denotes this probability, which signifies the probability of a difference at least as large as that observed being possible to arise by chance. The difference is designated significant when $0.001 < P < 0.01$, and probable when $0.01 < P < 0.05$.

CHAPTER VI

The Technique of the Electro-Shock Treatment

At the Psychiatric Clinic, up to the year 1953, use was made of the electroplexy technique indicated by MacPhail-Strauss. This method employs a monophasic or diphasic current measured in joules. In the majority of cases there was a monophasic current, only a minority of the patients being hard to shock and requiring a diphasic current. In some instances a mild sedative was administered prior to the shock, e.g. sodium amytal, and, exceptionally, curare.

Since the year 1953, ECT was carried out by means of the Siemen's "Konvulsator III nach v. Braunmühl": the effective value consisted of 300 mA, "Stufe 9", and the apparatus was adjusted to "unterbrochen". The time used generally varied between 2 to 6 seconds. This relatively high effective value was utilized in connection with shocks under narcosis of the apnoeic-diffusion oxygenation method introduced by M. Hᴉson Holmdahl, which is at present the method of routine at the Clinic. Approximately 45 minutes prior to the shock the patient was prepared with 0.25–0.50 mg of methylscopolamine nitrate ("Skopyl", Pharmacia) administered subcutaneously in order to obtain dryness of the mucous membranes of the air-passages and the mouth. The patient was made to breathe pure oxygen through a tight-fitting mask and was put to sleep through an intravenous injection of a short-acting barbiturate ("Narkotal", Astra, isopropyl-β-bromallyl-*N*-methylmalonyl carbamide sodium). About 0.3 g was injected during the course of 1 minute. Succinylcholine-iodide ("Celocurin", Vitrum) was quickly given through the same needle up to a complete muscular paralysis, about 0.8 mg/kg of body-weight. In order to avoid the risk of trombosis, especially in cases of poor veins, native saline was administered in addition to the injections. As apnoea set in during the muscular paralysis, pure oxygen was given, as a diffusion oxygenation, through a special pharyngeal tube applied to the patient. This was continued during the shock itself and the period after.

The patient was shocked about 45 seconds after the succinylcholine injection was completed. The duration of the shock was recorded by observing one of the patient's arms previously deprived of its blood supply and not affected by the relaxant. The method possesses certain advantages. The free airway diminishes the risk of complications in breathing in connection with the large doses of succinylcholine admin-

istered for the purpose of acquiring a complete relaxation of the muscles. The oxygen saturation of the blood is high, its lowest mean-value being 94.8 per cent (Holmdahl, 1953, oximeter readings in 48 shocks).

The shocks were given 2–3 times a week, independent of the method, and in the mornings, generally between 8.00–8.45 a.m.

CHAPTER VII

Experiments with Rabbits

The Choice of Animals and the Arrangement of the Investigations

An experimental study with animals, as to the effect of ECT on serum iron, was made for the purpose of offering the possibility of studying the biological effects of electro-shocks under conditions of physiological equilibrium and in "normal subjects". The clinical investigation of this work was to a great extent carried out on a material where an ordinary ECT has been employed accompanied by epileptic seizures. An effect on the serum-iron level of the el-shock was taken into consideration. Such an effect might be connected with a possible reticulocytosis. An increased number of reticulocytes could, among other causes, be brought about by the the cyanosis and lack of oxygen implied by the attack itself. In 1950 Riska, who has also reviewed current literature concerning the well-known problem of the lack of oxygen causing a reticulocytosis, found that a lowering of up to 8 per cent of oxygen of the air inhaled during as brief a time as four minutes gives rise to an immediate increase of the reticulocyte count in human beings, which disappears in a few hours, reappearing a few days later. The second increase was followed by an augmentation of the erythrocyte and haemoglobin values. In ECT the hypoxia during the post-convulsive apnoea, generally persisting during a period of 1–2 minutes, is pronounced. By utilizing an oxymeter, obtained by the kind assistance of Holmdahl (see above), values of the haemoglobinoxygen saturation, as low as about 60 per cent, were found in some of my patients who were examined by using the normal, non-modified ECT. Elderly individuals showed lower values. These results were in agreement with the findings by Holmberg and Lahne (1950) as well as those by Altschule *et al.* (1947).

Rabbits were used for the investigation. Concerning the use of rabbits, Heilbrunn and Weil found that the animals were hard to shock, only reacting with seizures when large doses of current were applied. Schmiterlöw and Silfverskiöld (1943) ascertained that rabbits were utilizable on administering a dose of the same amount as that used in human therapy. Also Bárány and his co-workers (1946) employed them

in experiments involving shocks. One drawback, however, is the fact that, in the severe extension of the tonic phase of their seizures, the rabbits sometimes break their backs, and become paralytic. Heilbrunn and Weil (1942) record the deaths of 16 rabbits out of 28 from paralysis, which mainly manifested itself in the hindmost parts of their bodies, affecting the evacuation mechanism of the bladder and the hind legs—a fact also experienced by the writer. (This occasionally occurs as a mishap on removing a rabbit from a smaller cage to a larger one, which offers the unexpected possibility of its making too high jumps initially uncontrolled.)

The advantages of using rabbits are several. They are large enough —an essential prerequisite for taking the required amount of blood, about 5 ml during repeated intervals. They have previously proved to be utilizable in the case of haematological and serum-iron investigations (Vahlquist *et al.*), and as classical animals for experimentation they are easy to handle, relatively cheap to obtain, and can above all be acquired in relatively homogeneous strains from those who cultivate them. Furthermore, rabbits are animals accustomed to living in cages and of a type that cannot be regarded as "stressed" during the course of experiments, as is, for instance, the case with cats, which, from the standpoint of shocks, offer certain advantages (Hartelius 1952).

The animals of white Swedish land-race employed in these experiments seemed to be of the same strain, and were relatively homogeneous, and from the same cultivator. They consisted of young males of 5–6 months of age, having a weight of approximately two kg each. The experiments were carried out during the periods of January–May and September–December. The food was homogeneous, having been ordered in two deliveries from the same supplier. Prior to the experiments, the animals were standardized for 3–4 weeks with the same food.

Their daily ration consisted of about 75 g of crushed oats and approximately 100–150 g of hay, a quantity which was seldom eaten the following morning, either by the control animals or by those treated. Fresh water in bowls of earthenware was changed every morning. The drinking-water of Uppsala is claimed to have a low iron content. The condition of the animals was carefully tested, also haematologically, and their weight once a week.

Methods.—Serum iron (SI), haemoglobin (hb.), red cells (Er.), reticulocytes (ret), and haematocrits (hct.) were determined by the same methods as those used on the clinical material. As to the determination of haemoglobin, according to Autenrieth-Königsberger, the method is applicable in the case of rabbit-blood without any special standardization (Barkan 1937, quoted by Vahlquist).

The Method of Blood Sampling.—Cardial punctures were used whenever serum iron was taken, and the remaining samples were

obtained simultaneously from a portion of an Ellermann tube having heparin exsiccated in a thermostat. Indifferent 2R2 needles were employed of a calibre of No. 12–14 and 60 mm long. The blood was generally collected in the centrifugal tube. On the whole the animals endured the puncture without any reaction whatever, during this operation itself or during the following day. In cases of accidents, the animals turned dyspnoeic and were shocked, dying some minutes subsequent to the experiment. Six animals of 125 punctured died in this way. In a few cases, an autopsy revealed haemopericardium and tamponade of the heart. In other cases, the blood samples were taken from a hyperaemic ear in the ordinary manner and with the stilet against a disc of cork. Rabbit-blood has a somewhat greater tendency to become haemolyzed than that of man. The haemolysis, however, was rather slight and as such does not affect the serum iron analysis.

The normal value of haematological data recorded by various authors is different. Other factors, besides the methods employed, that can play a certain rôle are hereditary strain, the composition of the food, and possibly the time of the year. Values found by the writer are recorded in Tables 1 and 2.

The ECT

The shocks were administered by the McPhail-Strauss plexacon apparatus (see above), and the electrodes were made in the form of clips having double electrodes slightly bent and made of brass-plate soldered to the arms of an alligator squeezer. Their size was 40 × 10 mm. They were wrapped in gauze and moistened with a 20 per cent NaCl solution as in clinical praxis. They were symmetrically applied to the anterior region of the ear, as portrayed in Figure 3, contacting the skull in the recess in front of the meatus acusticus externus. During the shock, the rabbit was suspended in a cloth having four holes for its legs, according to the figure.

Monophasic current was utilized. The doses used varied from 0.6–1.6 joules, usually 0.75–1.2, i.e. approximately the same dose in relation to the body-weight as is given in clinical practice. When the dose was below 0.6 joules, there were practically no epileptic seizures. As in clinical conditions with human beings, e.g. in mental maladies, a successive increase of the dose was required.

More than 100 shocks were administered—generally 8.30-10 a.m.—and in the ECT series all of them were effective and of the grand mal type. Every shock-treated animal was given 5 shocks during 10 days. Ten animals became paralytic and died in connection with the ECT. The dose applied was mainly low, and in subconvulsive reactions (*c.* 10 per cent) it was increased to about 10–20 per cent, whereupon the epileptic seizure set in. The attacks were most frequently, but not

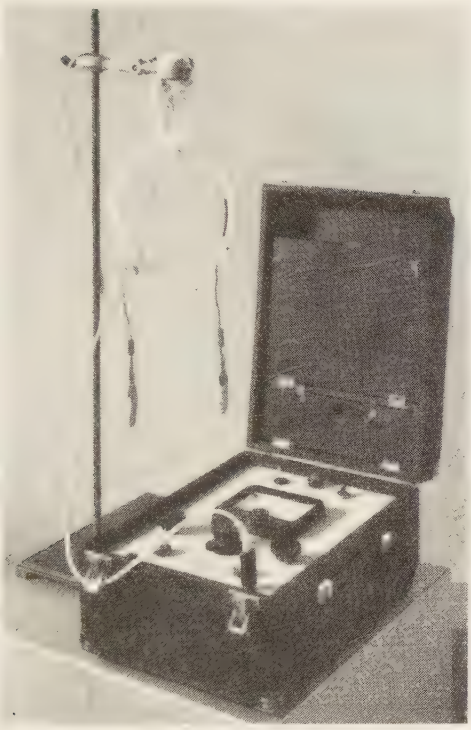

Fig. 2. The apparatus with the electrodes.

always, typical as well as symmetrical, requiring a certain degree of carefulness in the application of the electrodes. The arrangement given contributed to making the application of the electrodes more precise.

The latency period proved to be approximately 3–5 seconds; the tonic phase to be 10–15 seconds, starting with a flexion noticeable as a cranialward stretching of the forelegs and an adduction of the hind legs, passing over into an intense extension: the forelegs ventralward and the hind legs still more forcibly adducted and stretched backwards, the back being overstretched. During this tonic period a fine tremor could be felt in the muscles. There was a gradual relaxation of the tension, and the clonic phase of about 5–10 seconds appeared, consisting of syncronous and spasmodic movements. There was an increase, a maximum, and a decrease of their intensity, occasionally followed by running movements of the extremities. Afterwards the animals were in a state of coma lasting from 1/2 minute to some minutes. On awakening they seemed to be somewhat dazed. Quite fre-

Fig. 3. The tonic phase of the shock.

quently hyperirritability and hyperactivity were to be noted the first few hours following on the shock. As to vegetative reactions a horripilation could be observed.

Experiments and Results

The material of 40 animals, young males of a weight of about 2,300 g was divided into four groups consisting of ten each, and every group had two series, one as a normal series and one for treatment. The ten animals were at first standardized during a period of 3–4 weeks together with two animals in reserve to cover possible losses. Of the groups of 2×5 animals only one remained complete after the ECT, two of them consisting of 2×3 animals. With regard to a possible seasonal variation of the serum iron, the control and treatment values were taken at the same time. Most of the animals, however, belonged to the series from the spring, and there was no statistically significant seasonal variation in this material.

The volume of the blood samples taken was about 5 ml, hardly large enough to influence the serum-iron level representing about 3 per cent of the total blood volume (per kg of body weight, the same as 150–200 ml in man). The highest number of blood samples from the same rabbit was six, during a period of 4 months, and the interval between two punctures was at least 14 days.

In order to obtain a certain conception of *the fluctuations of the serum-iron level in rabbits*, 21 samples were taken from 8 rabbits, showing irregular variations of about 30 per cent in the same animal.

The question as to a diurnal variation of the serum-iron level is also of interest because one generally correlates the serum-iron level and sleep (see above), and because rabbits are regarded as having a polyphasic sleep-cycle. Samples were taken from 16 rabbits at 8–9 a.m. as well as at 3 p.m. Thus the difference was individual, but the samples were not taken the same day from the same individual (in accordance with the method). In spite of this and of the fact that the interval only amounted to 6 of the 24 hours of the day, a difference between the morning and evening values was ascertained.

As shown in Table 1, the difference between the individual values is 26 ± 10.3. Consequently it may be regarded as probable from a statistical point of view. This fact seems to justify the statement that there is a diurnal variation of the serum-iron level in rabbits.

A comparison between the serum-iron value and the haematological data prior and subsequent to the ECT, as well as after the first shock, is set forth in Tables 2, 3, and 4.

Certain values were also taken immediately after the ECT, 1 to 2 days after the treatment, from 16 animals (and all the values of minor interest from a few), according to Table 5.

The differences between the above means are recorded in Table 6.

As appears from Table 6, the serum-iron level is not changed within an hour after the first shock. The difference between a normal morning value and that of 1 hour after the first shock is -5.5 ± 18. A temporary tendency to an increase of the serum-iron level immediately

Table 1. Morning and afternoon values of serum iron, and haematological values and their individual differences in rabbits.

Values	Time	n	Mean values and differences			
			$M \pm \varepsilon (M)$	σ	$D \pm \varepsilon (D)$	σ
SI γ % . .	8–9 a.m.	16	261.7 ± 11.2	44.9	+ 26.0 ± 10.3	41.4
	15 p.m.		235.7 ± 12.4	49.8		
hb. g % . .	8–9 a.m.	19	12.21 ± 0.24	1.10	− 0.87 ± 0.54	2.34
	15 p.m.		13.08 ± 0.47	2.08		
Er. million	8–9 a.m.	19	4.64 ± 0.13	0.58	− 0.58 ± 0.26	1.15
	15 p.m.		5.22 ± 0.20	0.87		
ret. ‰ . .	8–9 a.m.	18	3.54 ± 0.32	1.37	− 0.16 ± 0.26	1.09
	15 p.m.		3.69 ± 0.34	1.46		
hct. % . .	8–9 a.m.	15	37.33 ± 0.86	3.31	− 0.97 ± 0.90	3.48
	15 p.m.		38.30 ± 0.92	3.57		

Table 2. Morning values (mean values) of serum iron and haematological values in rabbits.

Values	*n*	$M \pm \varepsilon M$	σ
SI γ%	20	265 ±10.6	47.4
hb. g%	30	12.33± 0.18	1.04
Er. million . .	29	4.5 ± 0.10	0.52
ret. ‰	28	3.19± 0.23	1.23
hct. %	19	37.23± 0.70	3.07

Table 3. Mean values one hour after shock as to serum iron and haematological values in rabbits.

Values	*n*	$M \pm \varepsilon M$	σ
SI γ%	21	270 ±14.5	66.2
hb. g%	19	12.70± 0.26	1.16
Er. million . .	10	5.33	—
ret. ‰	30	4.01± 0.16	0.90
hct. %	24	38.98± 0.89	4.34

Table 4. Mean values two weeks after ECT as to serum iron and haematological values in rabbits.

Values	*n*	$M \pm \varepsilon M$	σ
SI γ%	16	278±13.2	52.8
hb. g%	13	12.58± 0.38	1.39
Er. million . .	16	4.66± 0.12	0.48
ret. ‰	16	3.87± 0.32	1.29
hct.	16	38.10± 0.80	3.21

Table 5. Mean values 2–3 days after ECT as to serum iron and haematological values in rabbits.

Values	*n*	$M \pm \varepsilon M$	σ
SI γ%	16	293 ±13.4	53.6
hb. g%	7	12.18	
Er. million . .	11	4.64	
ret. ‰	16	3.77± 0.39	1.55
hct.	10	38.70	

Table 6. Differences between the means of serum iron and haematological values in rabbits according to Tables 2–5.

Values	Conditions	Diff. between the means
SI γ %	Normal morning value – 1 hour aft. 1st shock	− 5.5 ± 18.0
	» » » – 2–3 days aft. ECT	− 28.2 ± 17.1
	» » » – about 2 weeks aft. ECT	− 13 ± 16.9
hb.	Normal morning value – 1 hour aft. 1st shock	− 2.4 ± 2.1
	» » » – about 2 weeks aft. ECT	− 1.1 ± 2.8
	Within 1 hr. aft 1st shock – » » » » »	+ 0.8 ± 3.0
Er. million	Normal morning value – 1 hour aft. 1st shock	− 1.0
	» » » – about 2 weeks aft. ECT	− 0.13 ± 0.16
ret. ‰	Normal morning value – 1 hour aft. 1st shock	− 0.82 ± 0.28
	» » » – 2–3 days aft. ECT	− 0.58 ± 0.45
	» » » – about 2 weeks aft. ECT	− 0.68 ± 0.39
	Within 1 hr. aft. 1st shock – 2–3 days aft. ECT	+ 0.24 ± 0.42
hct. %	Normal morning value – 1 hour aft. shock	− 0.56 ± 1.04
	» » » – about 2 weeks aft. ECT	− 0.87 ± 1.06
	Within 1 hr. aft. 1st shock – 2 weeks aft. ECT	+ 0.88 ± 1.20

after the ECT in relation to the normal morning value is not to be found statistically in this small material, the difference being — 28.2 ± 17.1 (compare the individual differences below). The value of the serum-iron 2 weeks subsequent to the ECT reveals a good statistical agreement with the normal morning value. The difference is — 13 ± 16.9.

As to the other values, there is an increase in the number of reticulocytes immediately after the first shock in relation to the normal morning value. The difference is — 0.82 ± 0.28, thus being statistically probable, whereas no change is to be found 1 to 3 days after the ECT. The difference of the latter is — 0.58 ± 0.45. Nor is there any difference between the normal morning value and that of about 2 weeks after the ECT in my material (— 0.68 ± 0.39).

There is no modification of the red cells, apart from a possible momentary increase within 1 hour after the first shock. Besides this, no other changes of the red cells could be registered from the small material, nor did the haematocrit values show any alterations of statistical probability or significance.

With respect to the various values, according to their *individual* differences, see Table 7.

Table 7. Individual differences of values before, during, and after ECT as to serum iron and haematological values in rabbits.

Values	Conditions	n	$M \pm \varepsilon\,(M)$	σ	$D \pm \varepsilon\,(D)$	σ
SI γ %	Normal morning value Within 1 hr. aft. 1st shock	14	265.4 266.0		− 0.6 ± 11.9	44.7
	Normal morning value 2–3 days aft. ECT	9	255.9 304.3		− 48.4 ± 26.0	78.1
	Within 1 hr. aft. 1st shock 2–3 days aft. ECT	12	269.2 280.0		− 17.9 ± 27.4	95.0
	Within 2–3 days aft. ECT About 2–4 weeks ,, ,,	12	282.3 241.9		+ 40.4 ± 15.8	54.7
	Within 1 hr. aft. 1st shock About 2 weeks aft. ECT	12	262.9 259.4		+ 3.5 ± 23.3	80.6
hb. g %	Normal morning value Within 1 hr. aft. 1st shock	18	12.44 ± 0.26 12.64 ± 0.24	1.12 1.04	− 0.20 ± 0.37	1.55
	Normal morning value Within 2 weeks aft. ECT	12	12.47 12.42		+ 0.05 ± 0.47	1.65
	Within 1 hr. aft. 1st shock Within 2 weeks aft. ECT	12	12.70 12.64		+ 0.06 ± 0.47	1.64
Er. million	Normal morning value Within 1 hr. aft. 1st shock	9	4.91 4.51		− 0.50 ± 0.31	0.32
	Normal morning value About 2 weeks aft. ECT	9	4.81 4.49		+ 0.31 ± 0.18	0.53
	Within 1 hr. aft. 1st shock Within 2–3 days aft. ECT	8	5.54 4.81		+ 0.73 ± 0.18	0.51
	Normal morning value Within 2 weeks aft. ECT	14	4.63 4.54		− 0.07 ± 0.12	0.45
	Within 1 hr. aft. 1st shock Within 2 weeks aft. ECT	8	5.54 4.81		+ 0.73 ± 0.18	0.51
ret. ‰	Normal morning value Within 1 hr. aft. 1st shock	27	3.20 ± 0.24 3.94 ± 0.15	1.25 0.80	− 0.74 ± 0.26	1.33
	Normal afternoon value Within 1 hr. aft. 1st shock	20	4.05 ± 0.33 4.43 ± 0.17	1.47 0.77	− 0.38 ± 0.36	1.62
	Normal morning value Within 1–3 days aft. ECT	13	3.38 3.37		+ 0.02 ± 0.26	0.94
	Within 1 hr. aft. 1st shock Within 1–3 days aft. ECT	16	4.20 ± 0.23 3.77 ± 0.39	0.94 1.55	+ 0.44 ± 0.39	1.55
	Normal morning value About 2 weeks aft. ECT	13	3.38 3.50		− 0.11 ± 0.25	0.90
	Within 1 hr. aft. 1st shock About 2 weeks aft. ECT	16	4.20 ± 0.23 3.87 ± 0.32	0.94 1.29	+ 0.33 ± 0.31	1.25
	Normal morning value Within 2–3 days aft. punct.	10	2.95 3.20		− 0.25 ± 0.30	0.96
	Normal morning value 4–5 hrs. aft. 1st shock	11	2.70 2.86		− 0.16 ± 0.25	0.82
	Within 1 hr. aft. 1st shock 4–5 hrs. aft. 1st shock	11	3.61 2.86		+ 0.75 ± 0.24	0.81

Table 7 (cont.)

Values	Conditions	n	$M \pm \varepsilon(M)$	σ	$D \pm \varepsilon(D)$	σ
hct. %	Normal morning value Within 1 hr. aft. 1st shock	16	37.29 ± 0.70 37.63 ± 1.12	2.79 4.47	− 0.34 ± 0.82	3.26
	Normal morning value Within 1–2 days aft. ETC	7	36.87 36.86		+ 0.01	
	Within 1 hr. aft. 1st shock Within 1–2 days aft. ECT	10	37.80 38.70		− 0.90 ± 1.08	3.43
	Normal morning value About 2 weeks aft. ECT	8	36.14 37.06		− 0.93 ± 1.45	4.10
	Within 1 hr. aft. 1st shock About 2 weeks aft. ECT	15	38.93 ± 1.02 38.07 ± 0.86	3.94 3.32	+ 0.86 + 1.08	4.16

The serum-iron level did not show any statistically significant alteration. Nevertheless, there was a statistically *probable* difference of + 40.4 ± 15.8 between the value immediately after the ECT and that after 3–4 weeks. This would speak in favour of a temporary increase of the serum-iron level immediately after ECT. This is in accordance with the tendency of the other serum-iron values given in Table 7.

As to the reticulocytes, the increase after the first shock was manifested again in the individual differences, being 0.74 ± 0.26, which is statistically probable. The increase of the reticulocytes completely disappeared when the ECT was over.

After the initial shock there is a statistically probable and immediate increase, as shown above. The individual differences between the morning and evening values after the first shock (+ 0.75 ± 0.24) are statistically significant. The afternoon value (4–5 hours after the first shock) is however relatively low, and approximately the same as a normal one in the afternoon. This post-shock value also shows a good statistical agreement with the normal morning value, the difference being — 0.16 ± 0.25. This fact speaks in favour of a temporary outflow subsequent to and immediately after a shock, the reticulocytosis not being ascertained a few hours later.

In order to analyse the reticulocytes of each individual shock of the series, they were counted successively during the five shocks in 11 animals as shown in Tables 8 and 9.

The reticulocyte reaction is not pronounced at any time of the ECT. During the more than 50 shocks of this latter experiment no exceptionally high reticulocyte counts could be found.

To obtain an idea of the influence of ECT on the weight of the rabbits, the weights of 2 groups were compared in the case of 15 animals. The time of observation lasted 25 days. The animals were of about the

Table 8. Reticulocytes of 11 rabbits within one hour after ECT and about five hours after ECT subsequent to each shock, during the complete series of 5 shocks.

El-shock No.	Reticulocytes after el-shock, ‰			
	Value 1 hr. after el-shock		Value 5 hrs. after el-shock	
	n	Mean	*n*	Mean
I	11	3.73	6	2.83
II	11	3.82	11	2.68
III	11	3.55	10	3.40
IV	11	3.91	10	3.20
V	11	3.27	11	2.95

Table 9. Individual differences as to the reticulocytes of the successive shocks according to Table 8.

Diff. between shocks Nos.	Value 1 hr. after el-shock			Value 5 hrs after el-shock		
	n	$D \pm \varepsilon (D)$	σ	*n*	$D \pm \varepsilon (D)$	σ
I – II	11	-0.09 ± 0.31	1.04	6	$+0.33 \pm 0.28$	0.68
II – III . . .	11	$+0.27 \pm 0.27$	0.90	10	-0.70 ± 0.33	1.03
III – IV . . .	11	-0.36 ± 0.20	0.67	9	$+0.22 \pm 0.52$	1.56
IV – V . . .	11	$+0.64 \pm 0.24$	0.81	10	$+0.15 \pm 0.31$	0.97

same size with an average weight of 2,280 g in both groups. The two groups were run at the same time in subgroups of 5 + 5 animals, 2/3 of the material in spring, February–April, and the rest in November.

The series of shocks were given at the beginning of the tests during 10 days, by treating them every other day and on a few occasions every third day. The final weights of the treated animals were thus decided after an interval of 15 days without shocks.

The animals treated with shocks revealed an increase of weight, according to Table 10.

As is seen in the table, there is an increase of weight which, however, is not statistically confirmed from this small material.

Table 10. The increase of weight in 15 rabbits treated with ECT and in control animals, and differences of the mean weights.

Conditions	Time of observations (days)	n	Increase of weight, g	
			$M \pm \varepsilon (M)$	σ
Treated with ECT .	25.4	15	182.2 ± 23.4	90.8
Controls	25.3	15	112.8 ± 18.7	72.6
Differences in weight between ECT-animals and controls (g)			+69.4 ± 30.0	

Starvation Experiments

In order to obtain an idea of the influence of starvation on the serum-iron level, sixteen rabbits were divided into two groups, the first group being without water and food for 24 hours, whereas the second was allowed to drink, but not to eat, during a period of 48 hours. Samples for obtaining serum iron and the haematological values were taken at 8–9 a.m. on the second and the third day respectively. The animals of both groups did not seem to be exhausted by the experiments. Since the two groups did not show any mutual difference as to the various values, they are treated as a whole. The values acquired are to be found in Tables 11 and 12.

Table 11. Mean values of serum iron and haematological values, normal morning values and morning values after 48 hours of starvation.

Values	Conditions	n	$M \pm \varepsilon (M)$	σ	Differences between the means
SI γ %	Normal morning value Starvation value	20 17	265.4 ± 10.6 263.0 ± 12.4	47.4 51.0	+ 2.4 ± 16.3
hb. g %	Normal morning value Starvation value	30 7	12.33 ± 0.18 12.48	1.04	− 0.15
Er. million	Normal morning value Starvation value	29 16	4.53 ± 0.10 6.05 ± 0.16	0.52 0.66	− 1.52 ± 0.19
ret. ‰	Normal morning value Starvation value	28 16	3.19 ± 0.23 4.00 ± 0.24	1.23 0.97	− 0.81 ± 0.33
hct. %	Normal morning value Starvation value	19 17	37.23 ± 0.70 44.12 ± 1.00	3.07 4.12	− 6.89 ± 1.22

Table 12. Individual differences between normal morning values and starvation values as to serum iron and haematological values in rabbits.

Values	Conditions	n	$M \pm \varepsilon (M)$	σ	$D \pm \varepsilon (D)$	σ
SI γ %	Normal morning value Starvation value	10	275.4 256.4		+ 19.0 ± 16.9	53.4
hb. g %	Normal morning value Starvation value	7	12.42 12.48		− 0.06 − 0.4	
Er. million	Normal morning value Starvation value	15	4.39 ± 0.08 6.00 ± 0.17	0.29 0.64	− 1.61 ± 0.15	0.58
ret. ‰	Normal morning value Starvation value	16	2.87 ± 0.16 4.00 ± 0.24	0.65 0.97	− 1.13 ± 0.30	1.21
hct. %	Normal morning value Starvation value	10	37.90 42.55		− 4.65 ± 1.30	4.12

As appears from the tables, the serum-iron value after starvation reveals a good agreement with the normal morning values, the difference being + 2.4 ± 16.3. The individual difference of ten animals was + 19.0 ± 16.9. Hence, this is not in accordance with the fact that this type of starvation affects the serum-iron level in rabbits. On the other hand, the differences between the means of the haematocritic values and the erythrocyte counts, as well as the individual differences, speak in favour of an obvious haematodynamic variation in the direction of a haemoconcentration of statistical significance. The reticulocytes revealed a significant increase, as shown in the table.

It is of interest to note that the serum-iron level is kept practically constant during this form of stress, which brings about these other noticeable haematological alterations.

CHAPTER VIII

Viewpoints on the Differential Diagnosis of the Clinical Material

As in other countries, Swedish psychiatry has had clinics for neuroses for the last decade, in which many cases of endogenous depression of a mild and frequently non-psychotic type are treated. The actual material was solely collected from the Psychiatric Clinic of Uppsala during the years 1951–1953. As a State Hospital the Clinic admits patients from various parts of Sweden, especially central Sweden with a certain preponderance from districts adjacent to Uppsala. With a view to the severity of the malady, the material represents a selection, since the worst cases, including depressions of a highly psychotic character, are usually sent to mental hospitals. My intention was, by means of the diagnostics recorded below, to test whether any biological changes can possibly be recorded in this particular type of material.

According to experience in general and as indicated in the introduction, there occasionally arise great difficulties in limiting psychic diseases, in this case mostly pertaining to endogenous depressions of a manic-depressive type.

In his work, "Trauer und Melancholie", published in his Collected Works, 1913–1917, Freud dealt with the problem concerning the mechanism of the origin of natural sorrow and melancholia and their demarcation, applying his theory of the regression of the libido that passes over into narcissism. As a learned scientist he does not make any pretence of discussing a typical, unexceptionable and comprehensive material, but he touches upon the very borderline cases, thus, as he himself declares, depriving his reasoning of universal applicability in cases of melancholia. By these premises he claims, on the one hand, that "erst dieser Sadismus (viz. die unzweifelhaft genussreiche Selbstquälerei der Melancholie) löst uns das Rätsel der Selbstmordneigung". On the other hand, however, Freud asserts that "ein wahrscheinlich somatisches, psychogen nicht aufzuklärendes Moment kommt in der regelmässigen Linderung des Zustandes zur Abendzeit zum Vorschein", and this evidently also in these borderline cases of a "psychodynamic genesis".[1]

[1] As to endogenous and releasing factors respectively (here principally the influence of a psychotrauma on a psychodynamic interaction), the question of priority from an etiological point of view is of course not brought closer to its solution even in dealing

This limitation "upwards" in the direction of psychogenic and (not so severe) mixed conditions of a psychosomatic character—see my introduction—has been discussed in German literature partly in connection with "die vegetativ-dystone Depression (Hempel 1937)—in French literature "la depression neuro-vegetative". These mild borderline cases were discussed by Watts in 1947 as endogenous states of depression. In 1949 Chamberlain called them "cryptic depressive states", and in 1950 Campbell designated them mild manic-depressive psychoses, whereas Schou (1948) considered them to be a special malady.

Henderson and Gillespie (1952) assign some of these mild borderline cases to manic-depressive psychosis under the heading "Simple Depression". They emphasize the cyclothymic temperament and a family tendency to affective disorders, both being a support of the diagnosis. The difficulty of getting started in the mornings is stressed; changes of mood are not so apparent; but psychosomatic symptoms, such as dyspepsia, a bad taste in the mouth, and headaches of an ill-defined type are obvious. These milder forms of depression often occur under some other mask: "Such patients as these do not usually enter the portals of a mental hospital."

Jacobowsky took up the problem at the first World Congress of Psychiatry in Paris (1950) in his formulation of "endogenous forms of psychosomatic diseases." He emphasizes and summarizes a syndrome, which presents a synopsis of symptomatology possible to correlate with the biological kernel of the morbid process, and adds to this, conventional criteria (see below). He discusses the correlation of this condition with the manic-depressive nuclear group, and this was further developed by him in 1952.

He confirms the above diurnal rhythm also in these mild cases of endogenous depression, which had earlier been observed by Viggo Christiansen (1919), and later by Diethelm and by Müller, and which was used by Sargant (1950) as a condition for obtaining a good effect from ECT, i.e. a criterion of endogenous depression.

An endogenous diurnal rhythm consists of an accentuation of the malady and its symptoms in the morning, and a successive improvement during the day and in the afternoon, the patient falling asleep in a normal way, but sleeping restlessly after midnight, and awakening in the small hours, possibly in anguish.[1] This rhythm of sleep is in contrast to what is the case in neurotic depressions.

Common symptoms are those of the mucous membranes, such as dryness of the eyes, "lack of tears", thirst and dryness of the mouth

with psychoanalytic theories. See further my introduction on psychoanalysis as well as the footnote concerning the conception "endogenous".

[1] Independent of this *rhythm* of sleep, Lange stresses the incapacity for sleeping in conditions of depression, e.g. principally "zerhackter Schlaf" (of course in the small hours too), as an important *prodrome* in manic-depressive psychosis.

and throat—studied by amongst others Strongin and Hinsie (1938). These discomposures also manifest themselves as a loss of appetite, constipation, and gastro-intestinal disturbances, hypochylia being noticed by Hedström (1937). They are accompanied by loss of weight, this condition being an invariable symptom, according to Curran (modifying Gillespie) in his scheme of establishing differential diagnoses between endogenous depressions and neuroses—in line with traditional clinical experience. Another symptom to be adduced is the loss of libido and, occasionally, impotence. An additional fact to be observed in this work, indicating an endogenous process, is the accumulation of cases during spring and autumn; to quote Jacobowsky: "The condition should probably be interpreted as a change in the biotonus of the organism, a biologic vegetative-humoral alteration, which brings to mind Lange's ingenious comparison with the hibernation of certain mammals."[1] In this connection Jacobowsky (1953) deals with the hypothesis of a vagal block in mild forms of endogenous depressions, principally in connection with a ganglionic block experimentally caused by hexamethonium-iodide and -bromide.

As to the symptoms of inhibition, they are taken into consideration, referring to thought, the emotions, and the psychomotor functions. Frustation depressions were preponderant in relation to agitated ones. With regard to an occasionally transient component of agitation and a certain dissociation of the clinical picture, no division into these two groups is made, the reader being referred to the complete record of case histories in each specific case. Compare also the tendency to discard the too intricate subgroups in modern literature, as stated in my introduction.

As to the clinical picture, the writer regards the actual "Verstimmung", mainly on a constitutional basis, as the essential morbid trait. By this is meant the dominating change of mood in a depressive way, which is clearer in pronounced cases, and of greater intensity and duration than normal (i.e. in so far as the patient is unsociable and incapable of doing work), and *without any demonstrable lesional genesis of prominence.*

Concerning the differential diagnosis against asthenic "distemper", the latter possesses typical traits, viz. "reizbare Schwäche", and a different premorbid constitutional attitude towards life. Regarding the expectant-neurotic morning-fatigue of asthenics, it is more or less habitual and constitutional. The opposite condition is to be found in syntonic constitutions, which during periods of health are, as a rule, morning-active, as recorded in the case histories. During depressive

[1] The parallelism between this normal vegetative uneasiness which manifests itself more or less often, especially in the spring, as various psychosomatic reactions, and the religious formation and aspect of the Church Year with its Lenten and Passion season should be noted in this connection.

states, however, they seem to be "pseudoneurasthenic", brooding, and incapable of getting started in the mornings.

The cases bordering on schizophrenia are sometimes extremely difficult to distinguish, especially in conjunction with oligophrenia. Knowledge of the patient's age, his premorbid constitution, heredity, and lack of specific symptoms offer good help, but occasionally the diagnosis can only be made in the light of the subsequent course of the disease. In this connection it should be noted that an ECT administered in the case of an uncertain endogenous depression may reveal a fundamental schizophrenic process. The periodicity of the illness is to be regarded as a criterion—in the writer's opinion and in accordance with Müller (1936), who claims "die phasenhaft auftretende Gemütsstörung als Grundcharakter der Erkrankung".

Another central factor of diagnostics is that of age. Kraepelin designates the depression of middle age as melancholia, first as an independent group of maladies, then as belonging to manic-depressive psychoses (see my introduction). Bleuler includes involutional psychoses in this group in so far as they are typical and are dominated by the affective reaction. Quite laconically he states that "im Climacterium des Weibes zeigt sich eine kleine Häufung von Exacerbationen verschiedener Psychosen". In his monograph of 1952 on manic-depressive psychosis, Bellak adopts involutional psychosis under the heading "Allied Conditions" in conjunction with depressions of old age and manic-depressive psychoses occurring in connection with pregnancy. He follows the conventional division, implying that involutional psychoses "embrace affective reaction types which occur in women from the age of 40 to 55 years and in men from the age of 50 to 65 years". Bellak refers to the occasionally deviating clinical picture with an admixture of "schizo-phrenic-like and neurotic elements", the heredity being less pronounced than in manic-depressive psychoses (Brockhausen 1937, Palmer and Jardon 1941), but yet so obvious that it speaks in favour of a close affinity to this malady. He records the "psychosexual regression", the parallelism of which, in connection with the hormonal-endocrine involution, is discussed by Benedek (1950).

In short, the diagnostic criteria as well as the positive effect of ECT in typical cases justify, according to my opinion, a possible assumption of a biological (and enzymatic), common or similar, defective situation in these conditions of endogenous depression. They are also recorded as such in my material. The same is the case with typical conditions of endogenous depression in advanced age (e.g. in women after 55) as well as with those occurring in connection with pregnancy. The obvious influence of age on the clinical picture and on biological processes has, of course, never been denied. Compare Birnbaum (1920) who, in his "structural analysis", discusses pathoplastic and provoking factors in relation to pathogenetic ones in the formation of psychosis.

Amongst numerous other writers, this problem has been discussed by Sjöbring, who deals with his conception of "potentiality". In this context the psycho-analytical debate concerning libido should be mentioned, with its various types from different periods of life—apart from possible neurotic disturbances.

In short, the following criteria may be adduced, which can be used, with a certain amount of reliability, when diagnosing endogenous depressions, and which have been further developed by Jacobowsky (1950):

1. The heredity of periodical conditions of depression including manic-depressive psychoses.

2. Premorbid constitution, syntonic or cycloid, substable according to Sjöbring.

3. Previous depressions of an endogenous type, especially with an autumnal and vernal periodicity, as well as hypomanic (maniacal) reactions.

4. The clinical picture of the depression, the depressive syndrome: Inhibition symptoms with regard to thoughts, emotions (incidentally in the form of anaesthesia dolorosa), and inhibition of psychomotor activity. Endogenous diurnal rhythm, i.e. the depressive syndrome is more pronounced in the early morning, e.g. the incapacity for getting started then, in contrast to what is normal in the individual in question. A successive improvement towards the afternoon, falling asleep being normal, but incapacity for sleeping in the small hours; eventually, at times, anguish on awakening. Depressive vital symptoms of a psychosomatic character, loss of appetite, constipation, weakened sexual functions occasionally developing into impotence, symptoms of dryness of the mucous membranes such as diminished lacrimation, salivation, and hypochylia; a more or less pronounced loss of weight.

On the basis of the symptomatology in point 4 above, in a given case more or less complete in addition to at least one of the other premises 1–3, it is possible to establish a diagnosis of endogenous depressions with a likelihood that is probable with respect to the clinical premises of our day.

CHAPTER IX

The Clinical Material

The main material consisted of 39 patients suffering from endogenous depression (15 men and 24 women).

With regard to their *civil status,* 11 of the men were married, one a widower, and 3 unmarried (one of them being 21 years old). As to the women, 23 were married, and one a widow. Of the married men, 9 out of 11 had children—generally two—and of the women two were childless, the others having between 1 and 6 children, on an average 2.5 (11 women were of a fertile age, being 40 or less).

As for the *social status* of the patients, only two men had unqualified occupations, one being a labourer and the other a cattleman. Of those remaining, 5 were farmers on farms of their own, one a shop assistant in the business of his parents, one a foreman, one a house-painter, one a gardener, and one a barber, the three latter having a business of their own. Another was a fisherman, and two had more qualified work, one of them claiming university education.

As to the social status of the women, it may be observed that in 8 cases the husband had unqualified work, e.g. a saw-mill labourer, agricultural workers. Moreover, there were qualified workers, foremen, those who had independent occupations, and one with a high-school education.

As a rule, the patients were socially well adapted, living, with one or two exceptions, under good economic conditions.

Age distribution.—Of the men, 8 were fifty years of age, or less; two over 55. Of the women 15 were under 50, only 2 being in the age group over 60. This is shown in Table 13.

Table 13. Age distribution of the material.

Sex	Age groups, years.				
	21—30	31—40	41—50	51—60	61—65
Men	1	0	7	6	1
Women	5	7	3	7	2

Somatic type.—Seven men manifested predominantly pyknic traits; 7 were of an undecided type, occasionally with athletic traits, and in one case there were lepto-typic traits. The men were of an average height of 173.0 ± 1.6 cm ($\sigma = 6.1$), having a mean weight of 74.0 ± 1.3 kg ($\sigma = 5.1$) when admitted into the Clinic. The women revealed a pre-eminently pyknic constitution (15 cases); 6 were of an undecided type, and 3 were dysplastic. The mean value of their height was 162.4 ± 1.1 cm ($\sigma = 5.4$), and their mean weight 66.7 ± 2.6 kg ($\sigma = 12.6$). A few of them were a little corpulent, and one or two adipose.

With a view to their *earlier somatic diseases,* 3 of the male patients had periodical gastric disturbances in the form of ulcers (Cases 2, 6 and 13), one having been operated on (Case 6), one having suffered from a periodic gastritis, and one from a slight hepatitis (Case 11, his depressions occurred long before he contracted this malady). One man had undergone a gall-bladder operation, being one of the above ulcus patients (Case 6).

Of the women (Cases 3, 14, and 23) 3 had undergone gall-bladder operations (generally a single attack during the course of a depressive period, not accompanied by jaundice and operated on without complication). One of these female patients (Case 14) had also been operated on because of an ulcus ventriculi. Some patients suffered from hypochylia gastrica in connection with their depressive periods. One woman had been nursed for a couple of months at a sanatorium for a very mild t. b. pulm. Further, a minority of the patients had a slight hypertension, which often grew worse in connection with their anxiety states during their depressive periods (no changes of the eye-grounds were noticeable).

On the whole, the patients were physically healthy, apart from certain *psychosomatic disturbances* at the time of their depressions, which appeared as gastro-intestinal discomfort, pains of the back, palpitations of the heart, headaches, etc. The women mostly possessed a remarkably good capacity for work as soon as the depressions were over, and so did the men. Of the latter, 13 of 15, i.e. where there is a record, had completed their military training, and, in applicable cases, extra compulsory military service.

Severe cases of fever, as well as injuries of the brain of a traumatic, toxic, or infectious nature, were practically absent in the anamnesis. A couple of the patients had suffered from the Spanish flue in a very mild form and without noticeable complications in youth. One patient, however, revealed certain traits of the Parkinsonian syndrome appearing during his repeated depressions (Case 8). Furthermore, another man had parotitis epidemica at an adult age, preceding his first depression (Case 1).

A material comprising patients of the age groups represented here

and without any somatical diseases whatsoever would be artificial and almost impossible to obtain.

As to alcohol, there was no misuse, none of these periodic male patients being addicts. In my opinion, the difficulty of obtaining a more comprehensive and representative male material depends, among other circumstances, on the very fact that many men suffering from periodic depressions turn out to be alcoholics, and are recorded in social and medical statistics as belonging to this category.

The *releasing factors* of the depression of main interest are in this work considered to be of minor significance. In the male material, these factors were, for instance, heavy work and nocturnal duties (Case 4), or work in the height of the season (autumn), at the time when the habitual depressions of the patient generally appeared (Case 15), and as to the female patients, a not very harmonious marital relationship accompanied by childlessness and a post-climacterial situation (Case 2) ; the information that an unmarried daughter is pregnant (Case 3) ; an imbecile and troublesome son traumatizing a mother who is advancing in age (Case 6) ; a heavy burden of work in connection with illness in the family (Case 11) ; a husband who is incurable (Case 10) ; and a pregnancy (Case 4).

In these cases there are preceding depressions and other typical criteria of endogenous depressions.

As releasing factors, *infectious diseases* exclude the patient from the material where there is an obvious proximity between the malady and the mental depression. The homogeneity of the material is in this matter a necessary condition for carrying out an unobjectionable investigation into serum iron.

With respect to *sexual problems* as releasing factors, apart from the stress implied in the transitory depression itself, maladjustment is very seldom adduced. None of the women had pronounced disturbances of menstruation, not even during their depressive periods. Thus, in the female material, there is a husband who is an alcoholic with relevant problems (Case 1). In this case, however, the patient herself inherited periodic depressions, which had appeared from her youth. Moreover, there is disharmony in marriage, especially in the beginning, in connection with childlessness (Case 2) ; initially a lack of marital compatibility, which is soon overcome (Case 12 as well as Case 15), or a severe illness of the husband (Case 19). Further, there are very good marital relationships, none of the patients being frigid—a remarkable fact, considering the repeated number of rather severe depressions in many of them. With respect to the men, there is none who adduces "sexual problems". In the total material there is no instance of divorce. Concerning the

above data it may be stated that, as a matter of routine, the patients were examined by means of narco-analysis.

Heredity is a pronounced factor in the material. Nineteen of 39 patients (5 men and 14 women) revealed positive heredity, one of their parents, or brothers and sisters, manifesting periodical mental disorders, including alcoholism. In another 14 cases (6 men and 8 women) there was heredity, e.g. an uncle mentally depressed, or a grandparent having committed suicide in a fit of depression. Only 6 patients of these 39 (4 men and 2 women) disclaimed heredity as to nervous or mental diseases. In several cases heredity was confirmed on post-examination, the patient having made a more thorough investigation into his or her own heredity.

As to the *psychic constitution* of the patients, the majority of the men were pre-eminently extrovert (9 individuals), often having syntonic traits. Five were of a more indifferent type without any obvious divergence from the normal. In 3, pedantic traits could be discerned (Cases 1, 9, and 10), as well as a few cases being somewhat emotional. Apart from their periodicity, there were no apparent abnormal constitutions. They were as a rule of normal intelligence. One case, or possibly two, however, were debile.

With regard to the women, almost all were syntonic. Some are recorded as being somewhat emotional with a certain neurolability since childhood, e.g. enuresis (Cases 15, 17)—possibly trauma from their milieu, as well as in other analogous cases, which are in principle not taken up for discussion in this work. One had a slight anorexia as a child (Case 20); another, uneasiness in sleep (e.g. Case 11); a couple had developed late, having had menarche at 16–17 years of age (Cases 17 and 21), in the latter case with a familiar disposition. Moreover, a few were somewhat irritable premenstrually (e.g. Case 16). Nor was there, on the whole, any pronounced abnormal constitution among the women, apart from their periodicity. Their intelligence was good, with one or two exceptions of debility (e.g. Case 21).

The first appearance of the malady.—Most patients had suffered from earlier periods of depression prior to the one of chief interest. Seven men had gone through their first period, frequently of a non-clinical type, before their 30th year (Cases 2, 3, 4, 10, 11, 12, and 13) —a few of these as early as puberty. In the remaining cases, the depression first occurred at a mature age, not later than the age of 45. One (Case 15) had his first depression at the age of 46, but had before that time been typically moody in the autumns of the previous years. The same occurred, further, in a couple of other cases. In one or two instances (e.g. Case 2) the psychosomatic component was

initially predominant, and the depressive picture came to the fore during later years. Initial periodical gastric disturbances, where subsequently the depression takes the upper hand, were further to be found (Cases 6, 13).

Of the women, 12 patients had had their first depressions in youth, or before the age of 30. Of these there were three who at first had periodic gastric disturbances (Cases 4, 6, 14, the latter case subsequently complicated by gall-stone). Twelve patients had their first attacks at a mature age, the latest at about 40. The same applies to the men.

The number of depressions.—As to the number of preceding depressive periods, it may be pointed out that, in this connection, I include periods of depressive inhibition symptoms and broodings clearly indicated by the patient. As a rule the period required treatment by a doctor even though the patient was not sent to a mental hospital. Of the material, three men were treated for their first depressive attack (Cases 6, 9, 13). Other men had suffered from repeated depressive attacks amounting to about 5 to 7 periods (Cases 4, 8, 11), and the majority of the male patients were treated for their second or third period.

As far as the women are concerned, 5 patients were treated for their first period of a more pronounced character (Cases 1, 4, 7, 12, and 17), one for her seventh period (Case 3), and another having even had 8 to 10 preceding periods (Case 10), the latter case being practically treated continuously with ECT at the mental hospital. Also with regard to the women, the period of chief interest was the second, or the third.

With respect to *the length of the period*, the time of *duration before admission* into the hospital was, in the case of men, up to approximately one year (Cases 2, 3, 4), there being as a rule three months of anamnesis before the admission of the patient (Cases 1, 10, only one month).

Regarding the women, 4 patients had a rather lengthy anamnesis in connection with the period of main interest (Case 2 having nine months, Case 12 eleven, Case 22 fourteen, Case 11 about eighteen). In other instances, the anamnesis was 1–6 months, generally 2–3.

Concerning the total number of cases of both sexes, it may be pointed out that the depressive periods developed successively, sometimes remaining constant prior to the patient's admission to hospital, there being in some cases an exacerbation necessitating this admission. In a few instances there was a fluctuating precurrent picture, especially where there was a lengthy anamnesis. Exceptionally (Case 18, a woman) the period was in an obvious remission, the patient recovering

without treatment a couple of weeks after her admission into the hospital.

The time of nursing at the Clinic amounted, on an average, to just under two months with regard to men, and approximately two months in the case of women.

As for the *clinical picture,* the patient was, as a rule, not severely psychotic. A certain disorientation is recorded in one male case (Case 1), who, similar to case 6, manifested more psychotic traits in a later depression. A certain mild confusion could not be excluded in Case 4. Among the female cases there was a certain dullness of mind with pronounced delusions of sin (Case 2) and attempts at suicide (Cases 20, 24) requiring their admission into the hospital. In one case (Case 20) there were temporarily traits of "Beziehungswahn". Besides that, there was no splitting, nor disintegration of a noticeable degree, nor hallucinations.

On the whole, the patients revealed a picture of *frustration depression,* there being, strictly speaking, no agitated patient in the material. The men showed an endogenous diurnal rhythm, i.e. with an improvement of their inhibition symptoms towards the afternoon in 12 of the 15 cases (except in Cases 2, 5, and 9). There were difficulties in sleeping, predominantly in the small hours, except in Cases 5, 10, and 11, where the incapacity for sleeping was less pronounced. Sleep was not continually disturbed every night in the cases recorded, but the tendency was there, more or less. With respect to the women, all had an endogenous diurnal rhythm as to their inhibition symptoms, and the majority an incapacity for sleeping of the endogenous type. An exception was Case 20, and further Cases 1, 5, and 10.

Concerning *symptoms of the mucous membranes,* 29 individuals of the entire material showed positive findings in the form of dryness of eyes or mouth, thirst, and constipation. Of the men, the following cases were exceptions: Cases 2, 4, 7, 10, 11, and 13; of the women, Cases 4, 7, 16, 20, and 22. *Psychosomatic symptoms* in the form of gastro-intestinal disturbances, palpitations of the heart, pains in the back, and so on, occurred frequently in the material.

There was almost always a *component of anguish,* more pronounced in the mornings and, at the same time, concomitant with distinct symptoms of inhibition, occasionally replacing the latter.

Body-weight.—It may be worth mentioning that these generally well-nourished patients revealed an insignificant or moderate loss of weight of 1–3 kg in connection with their periods of depression. In two cases, a woman (Case 21) and a man (Case 2), there was an obvious loss of weight of 10–15 kg. In the latter instances, the patients

were in their climacteric age, being 46 and 51 respectively. Previously they were rather obese, still weighing 56 kg and 73 kg, with a height of 156 and 169 cm, respectively, on being admitted into the Clinic, both being somewhat below normal height.

A remarkable fact is that the mean weight of the patients did not increase in any noticeable way during their stay at the Clinic and during the period of recovery. A synopsis is given in the form of a table in the following chapter dealing with laboratory data.

The methods of treatment.—All of the male patients were given el-shocks—the first 6 patients ECT, and the remaining 9 el-shocks under narcosis of the apnoeic-diffusion oxygenation method, described in Chapter VI. The series of shocks were brief, generally comprising 4 to 5 shocks two or three times a week. In a few cases a supporting sedative insulin treatment was applied.

Eighteen of the 24 female patients were treated with el-shocks, 12 being ECT (Cases 2–12, and 23) and 6 el-shocks of the above oxygenation method (Cases 14, 15, 17, 21, 22, and 24). Two individuals were administered histamine as the chief method of treatment (Cases 13 and 19), which was also applied to a couple of patients receiving el-shocks.

As with the male patients, sedative insulin treatment was also given to the women as a means of support. In three instances (Cases 1, 16, and 20) sedative insulin treatment in connection with opium was applied. One case (18) was remitted spontaneously after one or two weeks' sojourn at the hospital without any direct treatment. Her period was on the decline on her admission into the Clinic. Opium and sedatives were given to most patients.

The results of treatment.—With a view to *the immediate results* of the treatment, all 39 patients had recovered or improved when discharged from the Clinic. On their *post-examination,* 3 months to $2\,^1/_2$ years subsequent to their discharge, 2 men (Cases 2, and 6) were incapable of work and could not be considered recovered. Furthermore, during the interval, another 2 men (Cases 1, 10) had suffered from new periods of depression, but were on the whole healthy on post-examination. One male patient (Case 13) had improved, but had not resumed his work to the full extent. On post-examination of the women, 1/2 to $2\,^1/_2$ years after their stay at the hospital, one patient had to be treated again at a mental hospital (Case 6), and another had a new attack of depression coming on (Case 7). One female patient revealed a certain degree of psychic rigidness, not being quite healthy, but capable of working (Case 3). Another woman had in the meantime suffered from new periods of depression requiring ECT, but

had recovered when post-examined. Moreover, one patient had been hypomanic for a couple of months (Case 12), but she too had recovered.

In all, 2 patients remained ill, 1 recently relapsed into a depression, and another 2 had not fully recovered.

CHAPTER X

Laboratory Findings

A. Endogenous Depression

1. Serum iron and the total iron-binding capacity

Concerning normal values.—As was maintained in Chap. III, serum iron manifests a significant decrease before the 50th year. My clinical material mainly belonged to mature or middle age, which is also in accordance with the nature of the malady, which shows its greatest frequency in these years. My endeavour was to obtain a normal material of approximately the same distribution of age. It comprised some male and female nurses, a couple of my colleagues, and others, the majority constituting industrial workers having various types of work. All these individuals were healthy without recently having had any infectious disease. The normal values are recorded in the table below (Table 14). The values refer to fasting values at 8 a.m. The mean age of the male material amounted to 40 years, and that of the females to 32. Other normal values are to be found in Tables 14 a and 14 b.

The procedure in taking the *clinical* samples was the following. The patients were fasting, and the samples were taken between 8 and 8.30 a.m., apart from those representing the diurnal rhythm curve. Before taking the latter samples, the patients had had their regular meals—breakfast at 9, lunch at one, and dinner at 6. With a few exceptions, the patients were not confined to bed, and all of them had been up making their morning toilets prior to taking the 8 o'clock samples. On the days when the tests were made, the patients were not administered any medication, and only in a few cases had they been given some mild and short-acting soporific. Even during the days immediately preceding this, they had not received any strong sedatives. In this respect the patients had obtained the same regimen at the time of taking their values of health and illness. No patients were psychotic to the extent that they revealed negativism in the form of refusing food.

As it proved to be difficult to obtain a representative male material within a reasonable period of time, the investigations were concentrated on the female material, the malady also being considered mainly a female one.

As the patients have a more or less marked inhibition before noon and an improvement in the afternoons, it was considered justified to

Table 14. Serum iron (SI), total iron-binding capacity (TIBC), and their quotient (SI/TIBC). Normal values.

	n	SI gamma per cent		TIBC gamma per cent		SI/TIBC per cent	
		$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ
Men	24	130.8 ± 4.8	23	321.4 ± 6.2	30	41.0 ± 1.7	8
Women . .	26	124.2 ± 3.9	20	318.3 ± 3.7	19	39.0 ± 1.1	6
Both sexes .	50	127.4 ± 3.0	21	319.8 ± 3.5	25	40.0 ± 1.0	7

Table 14 a.[1] *Haemoglobin, erythrocytes, haematocrits, and reticulocytes. Normal values.*

	n	hb., g%		Er., mill.		hct., % (corr. 0.95)		ret., ‰	
		$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ
Men . .	15	15.24 ± 0.23	0.9	4.81 ± 0.08	0.3	43.3 ± 0.60	2.3	4.27 ± 0.21	0.8
Women	20	13.93 ± 0.19	0.8	4.40 ± 0.05	0.2	39.2 ± 0.44	2.0	4.63 ± 0.20	0.9

[1] 15.6 g % = 100 % Hb.

Table 14 b. Serum protein. Normal values.

	Serum protein per cent		
	n	$M \pm \varepsilon(M)$	σ
Men	24	7.50 ± 0.13	0.6
Women	26	7.10 ± 0.14	0.7

take samples at 8 a.m., noon, and a little before 5 p.m. In normal conditions, the serum-iron level presents a decline during the day.

In several cases the values of illness and health refer to 2 different days respectively. In some single cases the value of illness represents the mean value of 3 different days in the same patient.

The unsaturated iron-binding globulin refers to the morning-fasting value of the day when the corresponding serum-iron value was obtained, jointly constituting the TIBC.

The haematocrit values, the values of the serum protein, as well as the haematological values, were determined on the same blood samples as the serum tests for iron and iron-binding globulin. Venal punctures were made by means of indifferent 2R2 needles, and the blood was received in a centrifugal tube (*c.* 3–7 ml) and an Ellermann tube with exsiccated heparin. The blood was extracted with the greatest care—

Table 15. Serum iron in endogenous depressions. Women.[1]

Case No.	SI gamma per cent		
	8 a.m.	Noon	5 p.m.
1	205.0	—	—
2	137.5	156.5	156.5
3	161.0	188.0	157.0
4	194.5	155.0	160.0
5	189.5	200.0	191.0
6	186.0	172.0	142.5
7	206.5	228.0	208.0
8	144.7	158.0	78.0
9	217.0	161.0	152.0
10	147.0	154.0	122.5
11	190.0	167.3	155.0
12	168.5	151.0	90.0
13	163.7	158.0	140.3
14	153.0	150.0	135.0
15	132.0	120.0	62.0
16	198.0	223.0	182.0
17	223.0	193.0	156.0
18	148.0	173.0	191.0
19	161.5	148.0	127.0
20	151.0	200.0	143.0
21	128.0	129.0	93.0
22	161.0	157.0	182.0
23	125.0	132.0	139.0
24	172.3	125.5	95.5

Time	Number of cases	SI gamma per cent	
	n	$M \pm \varepsilon(M)$	σ
8 a.m.	24	169.3 ± 5.8	29
Noon	23	165.2 ± 6.0	29
5 p.m.	23	141.7 ± 8.0	38

the Ellermann tube being the first to be filled—and the work was carried out practically without any stasis, the blood being allowed to flow spontaneously into the tubes.

As appears from Table 15, the serum-iron level of illness reveals a relatively high morning value, viz. 169.3 ± 5.8 gamma per cent (compare the distribution of age and the decrease of serum-iron even before middle-age). This value differs significantly from the normal value in women, the difference being 45.1 ± 7.0 gamma per cent.

[1] The values represent mean values of 1–3 (4) successive days, as in Tables 16, 17, 19, and 28.

Table 16. Serum iron in endogenous depressions. Men.

SI gamma per cent			
Case No.	8 a.m.	Noon	5 p.m.
1	139.0	154.0	121.0
2	214.0	159.0	116.0
3	141.5	142.0	112.0
4	208.0	132.0	108.0
5	213.0	256.0	189.0
6	173.0	175.0	144.0
7	176.0	174.0	146.0
8	186.5	185.0	118.0
9	221.0	—	—
10	282.0	—	—
11	172.0	167.0	166.0
12	216.0	163.0	132.0
13	227.0	—	—
14	270.0	—	—
15	151.0	173.5	143.5

Time	Number of cases	SI gamma per cent	
	n	$M \pm \varepsilon (M)$	σ
8 a.m.	15	199.3 ± 11.0	43
Noon	11	171.0	
5 p.m.	11	136.0	

The variation of the serum-iron level of the same patient amounted to 20–30 gamma per cent from one day to another.

From Table 15 *the diurnal rhythm* of the serum-iron level is simultaneously obtained with regard to the 24 female patients suffering from endogenous depressions.

Similarly, the serum-iron value of 15 depressed male patients was determined, as shown in Table 16.

As is to be seen in the table, these male individuals, too, reveal a remarkably high morning value of serum iron, viz. 199.3 ± 11.0 gamma per cent. The difference between this value and the normal morning value is, in the case of men, + 68.5 ± 12.0 gamma per cent, thus being statistically significant.

As to the female material, their diurnal variation of serum iron during the day was examined on recovery (or improvement), Table 17. The stay of the patients at the clinic had then been 2 months, on an average. Most of them had been treated with ECT, some with insulin, and a few with histamine.

Table 17. Serum iron. Values of illness and health in women.

Case No.	SI gamma per cent					
	Illness			Health		
	8 a.m.	Noon	5 p.m.	8 a.m.	Noon	5 p.m.
1	205.0	—	—	107.7	114.0	98.0
2	137.5	156.5	156.5	131.0	107.0	102.5
5	189.5	200.0	191.0	134.0	116.0	99.0
6	186.0	172.0	142.5	134.0	110.5	101.5
8	144.7	158.0	78.0	123.0	109.0	95.0
9	217.0	161.0	152.0	121.0	146.0	120.0
10	147.0	154.0	122.5	108.0	95.5	74.0
11	190.0	167.3	155.0	122.0	115.5	85.0
12	168.5	151.0	90.0	145.0	112.5	94.5
14	153.0	150.0	135.0	121.0	98.0	65.0
15	132.0	120.0	62.0	116.0	106.5	116.0
17	223.0	193.0	156.0	108.0	90.0	87.0
19	161.5	148.0	127.0	150.0	164.0	140.0
21	128.0	129.0	93.0	152.0	152.0	118.0
23	125.0	132.0	139.0	108.0	109.0	82.0
24	172.3	125.5	95.5	103.8	96.0	82.7

As appears from Table 18, the serum-iron level of the patients on their recovery amounts to approximately normal values, i.e. 124.0 ± 3.9 gamma per cent. A comparison between values of health and illness is drawn up in the table. The individual differences of these values of health and illness (Table 18) amount to — 43.5 ± 9.5 gamma per cent, thus being statistically significant. Also the noon value, which is relatively high during illness, indicating a very insignificant drop in relation to the morning value of illness (a level curve), revealed a difference between the healthy/ill values amounting to — 39.3 ± 8.7 gamma per cent. Consequently, this difference is approximately as great as that of the corresponding morning values, and is also statistically significant. Turning to the evening values, we find that, during this time of the day when the patients are in a relatively good condition, even when ill, there is no significant difference between the values of healthy/ill. (The depressive inhibition of the patients was then, as a rule, not obvious, being in the majority of cases absent.)

The decline of the serum-iron value might possibly be regarded as a temporary and transitory reaction in connection with the biological transformation in close relation to recovery. It is possibly an effect of the treatment itself. The patients showed this decrease of their serum-iron levels independent of the method of treatment used. This argues for the assumption that the method of treatment *per se* plays a subordinate rôle in bringing about the decrease of serum iron. (However,

Table 18. Serum iron in women: Individual differences between values of health and illness.

	Time	Number of cases	SI gamma per cent	
		n	$M \pm \varepsilon(M)$	σ
Illness	8 a.m.	16	167.5 ± 7.9	32
	Noon	15	154.5 ± 5.9	23
	5 p.m.	15	126.3 ± 9.2	36
Health	8 a.m.	16	124.0 ± 3.9	16
	Noon	15	115.2 ± 5.6	22
	5 p.m.	15	97.5 ± 5.1	20

Individual differences: Health/Illness.

Time	n	$D \pm \varepsilon(D)$	σ
8 a.m.	16	−43.5 ± 9.5	38
Noon	15	−39.3 ± 8.7	34
5 p.m.	15	−28.9 ± 11.1	43

it should be noted that most patients were given el-shock treatments.) The question as to whether the serum-iron decrease only implies a temporary decline during the few weeks of recovery would mean, if answered in the affirmative, that the patients, in ordinary conditions, represented a *constitutionally* high serum-iron level.

In order to obtain an answer to this question, the serum-iron value of the female patients who are on the whole healthy was examined $^1/_2$ to $2\,^1/_2$ years after their period of infirmity. Thus, 15 of the 24 female cases were post-examined. For practical reasons, only patients from Uppsala and adjacent districts could be examined. A diurnal curve was taken of their serum iron. The values are recorded in Tables 19 and 20.

As appears from the table, these patients manifest normal values, the morning one being 133.1 ± 6.2 gamma per cent. At this time there was a statistically significant difference in relation to their high values during depression, i.e. with respect to their high *morning* values: — 35.1 ± 8.5, the difference being probable at noon, but the postexamination/ill values agreeing statistically rather well in the afternoon, according to Table 20. All the differences are individual, but do not include all the patients recorded in Table 17, comprising the values of health on their discharge from the hospital immediately after their recovery. Alternatively, most of the 24 patients have health or post-examination values.

Table 19. Serum iron in women. Values of illness and post-examination.

Case No.	Illness			$^1/_2$–2 $^1/_2$ yrs. later (Healthy)		
	8 a.m.	Noon	5 p.m.	8 a.m.	Noon	5 p.m.
1	205.0	—	—	113.0	89.0	77.0
3	161.0	188.0	157.0	132.0	188.0	187.0
4	194.5	155.0	160.0	122.0	139.0	105.0
5	189.5	200.0	191.0	126.0	90.0	80.0
9	217.0	161.0	152.0	153.0	153.0	106.0
10	147.0	154.0	122.5	123.0	170.0	146.0
12	168.5	151.0	90.0	169.0	181.0	126.0
13	163.7	158.0	140.3	168.0	162.0	124.0
14	153.0	150.0	135.0	132.0	144.0	126.0
15	132.0	120.0	62.0	71.0	64.0	47.0
16	198.0	223.0	182.0	138.0	123.0	85.0
18	148.0	173.0	191.0	132.0	125.0	101.0
19	161.5	148.0	127.0	129.0	108.0	101.0
20	151.0	200.0	143.0	165.0	105.0	135.0
21	128.0	129.0	93.0	147.0	131.0	122.0
24	172.3	125.5	95.5	109.0	50.0	46.0

Table 20. Serum iron in women: Individual differences between values of post-examination and illness.

	Time	Number of cases	SI gamma per cent	
		n	$M \pm \varepsilon(M)$	σ
Illness	8 a.m.	16	168.2 ± 6.5	26
	Noon	15	162.4 ± 7.6	30
	5 p.m.	15	136.1 ± 10.0	39
$^1/_2$–2 $^1/_2$ yrs. later	8 a.m.	16	133.1 ± 6.2	25
	Noon	15	128.9 ± 10.4	41
	5 p.m.	15	109.1 ± 9.4	36

Individual differences: Post-examination/Illness

	Time	n	$D \pm \varepsilon(D)$	σ
	8 a.m.	16	−35.1 ± 8.5	34
	Noon	15	−33.5 ± 11.7	45
	5 p.m.	15	−27.0 ± 12.2	47

Table 21. Serum iron (SI), total iron-binding capacity (TIBC), and their quotient (SI/TIBC) in endogenous depressions (females).

	No. of cases	SI gamma per cent		TIBC gamma per cent		SI/TIBC per cent	
	n	$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ
Women	21	173.4 ± 6.1	28	351.4 ± 14.2	65	51 ± 2	11

In consideration of the individual values of the patients, it may be noted that those who possess the highest values on being post-examined (Table 19), and somewhat below 170 gamma per cent (Cases 12, 13, and 20), are the following: Case 12, the patient having suffered from a hypomanic reaction in the summer of 1953. She was during the exploration somewhat tense. Case 13 had been working very hard, was strained, and had not slept well during the night prior to her post-examination. Case 20 was the patient whose clinical picture temporarily verged towards "Beziehungswahn".

The relatively high values are, of course, not remarkable *per se*, but are worth mentioning in connection with what is stated below. Of the few male patients post-examined with iron curves, 4 of those healthy revealed a morning value of approximately 130 gamma per cent; 2 who had not fully recovered (Cases 10, and 13) manifested a value of 197 and 199 gamma per cent respectively (see the case histories).

As to *the iron-binding capacity of serum*, illness and health values of most of the patients were taken. As is to be seen in Table 21, the patients reveal no great deviation from what is normal.

This table indicates that the TIBC is within normal limits. The unsaturated part of the iron-binding globulin is relatively small, and the normal quotient of saturation of approximately 1/3 is transformed, in cases of depression, into more than 1/2, the greatest part of the globulin being saturated.

2. Other laboratory findings

In order to obtain a picture of the *general condition of the patients*, notably with regard to their weight, haematological situation (haematocrit values, haemoglobin, red cells, and reticulocytes), including their water-metabolism, the following investigations were made. Knowledge of this is of importance in explaining the changes of the serum-iron level.

Regarding the body-weights of the patients, the majority show one or two kg loss of weight during their depressions. The anamnesis of the patients before their being admitted to the clinic was, as recorded in

Table 22. Body-weight. Values of health and illness in men and women.

	Weight, illness (kg)			Weight, health (kg)	
	n	$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ
Men	15	66.7 ± 2.6	12.6	66.6 ± 2.4	11.6
Women	24	74.0 ± 1.3	5.1	74.8 ± 1.2	4.5

Indiv. diff.: Health/Illness (kg)			
	n	$D \pm \varepsilon(D)$	σ
Men	15	$+0.87 \pm 0.49$	1.89
Women	24	$+0.08 \pm 0.46$	2.2

Chap. IX, generally a few months. The drop of weight occurring in most cases is remarkably moderate; and, furthermore, the patients are well nourished and did not show any signs of bodily degeneracy when admitted to the hospital in these mild forms of depression. (Their turgor was obviously on the decline.)

One female patient, however, indicated an extremely great loss of weight—about 10 kg (Case 21). In this case her decrease had occurred during a period of about 4 months (her serum-iron value was not high, being 128 gamma per cent). However, it is of course impossible to obtain exact data about the loss of weight of the patients prior to admission. On the other hand, the increase of weight during their recovery and sojourn at the hospital was obtainable, and is of great importance. These values are given in Table 22.

As appears from the table, the women showed practically no increase of weight during their stay at the hospital, the difference between the health/illness values being $+ 0.08 \pm 0.46$ kg. As for the men, there is a slight increase of weight, amounting to 0.87 ± 0.49 kg.

The *haematocrit values,* which during the illness of the patients might indicate a haemo-concentration, are within normal limits, as shown in Table 23. The health values represent somewhat lower ones within normal limits.

The values of haemoglobin, erythrocytes, and reticulocytes are also within normal limits, as is shown in table 24.

The differences between values of illness and health argue for a moderate increase of these haematological data.

It may be noted that all the patients manifest relatively good blood values. It should be kept in mind that, normally, the patients represent well-nourished and active pyknic types. Prior to their admission to

Table 23. Haematocrit values. Individual differences between health and illness in endogenous depressions.

hct., % (corr. 0.95)					
	Illness			Health	
	n	$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ
Women	15	41.45 ± 0.44	1.7	39.05 ± 0.40	1.6
Both sexes . . .	23	42.42 ± 0.48	2.3	40.39 ± 0.63	3.0

Indiv. diff.: Health/Illness			
	n	$D \pm \varepsilon(D)$	σ
Women	15	− 2.40 ± 0.47	1.8
Both sexes . . .	23	− 2.02 ± 0.46	2.19

Table 24. Haemoglobin, erythrocytes, reticulocytes, and serum protein. Individual differences between health and illness. Women.

	Values of hb., Er., ret., and serum protein (women)						
	n	Illness		Health		Indiv. diff.	
		$M \pm \varepsilon(M)$	σ	$M \pm \varepsilon(M)$	σ	$D \pm \varepsilon(M)$	σ
Hb. g % . . .	20	13.37 ± 0.17	0.8	13.89 ± 0.24	1.1	+ 0.52 ± 0.21	0.9
Er. mill. . . .	20	4.01 ± 0.08	0.4	4.30 ± 0.08	0.4	+ 0.30 ± 0.09	0.4
Ret. ‰	22	4.80 ± 0.41	1.9	6.02 ± 0.38	1.8	+ 1.23 ± 0.38	1.8
Serum protein %	19	7.18 ± 0.15	0.7	7.56 ± 0.16	0.7	+ 0.38 ± 0.22	0.98

the clinic and since the depression set in, however, they had had periods of poor appetite and malnutrition.

Serum-protein values show no essential deviations from the normal. The values of illness were somewhat lower than those of health, a fact that does not speak in favour of a dehydration of the blood.

A study of the *plasma volume* gives the following values by applying Evans blue dye method (see Table 25).

As can be seen from the table, depressive patients reveal, on using this relatively inexact method, values within normal limits. It should be noted that the patients are older than the material from which the normal values are obtained. What is interesting in the table are the few individual differences recorded. They all show a very slight tendency to increase on the recovery of the patients.

Table 25. Plasma volume in endogenous depressions.

	Plasma volume		
	n	ml/kg body weight	Normal value, ml/kg
Men	5	48	46.6
Women	10	43	44.9

Mean value of 8 indiv. diff.: Health/Illness $= +335 \pm 115$ ml ($\sigma = 324$).
Plasma volume, mean value of the eight cases = 2,880 ml.

The diuresis of the patients during illness and on their recovery is of some interest. A test was made of the diuresis during the day and the night, as well as of the specific gravity of the urine. Tests were made on 19 patients, mostly during a period of 2 to 3 days and nights. Ten individual differences were obtained. The values are given in Table 26.

As appears from the table, the amount of urine is less during depression, and the difference between day and night is not so marked, the specific gravities being about the same both day and night. On the recovery of the patients, the quantities of urine increase, especially in the day. The difference between day and night is now more pronounced.

Acute infections causing fever and a concomitant rise of the SR brought about a drop of the high serum-iron level in endogenous depressions (4 cases).

A minority of the patients were examined during *repeated depressive periods*, e.g. Cases 19, 22, and 23. Furthermore, there were patients not included in the main material. One of these who had a depressive period of temporary confusion, the diagnosis schizophrenia not being possible to ascertain, was successively examined from December 1950. She was a woman in her involutional age, born 1900. In her obviously periodical and depressive periods, her serum iron was generally above 200 gamma per cent (max. 222 gamma per cent). In periods of health she presented values of 100 to 140 gamma per cent. Some female patients treated policlinically for mild autumnal and vernal depressions possessed a serum iron of 150 to 180 gamma per cent in depressive conditions, whereas, on recovery, their values dropped to about 100 gamma per cent. A male depressive patient having an obvious inherited tendency to periodic mental deficiency revealed a serum-iron value of 218 gamma per cent. After being treated with ECT, he was considered fit for discharge, but relapsed into his depression, and was re-adminis-

Table 26. Volumes and specific gravities of urine in endogenous depressions. Women.

	Night						Day					
	Volume, ml			Spec. gravity			Volume, ml			Spec. gravity		
	n	$M \pm \varepsilon(M)$	σ	n	$M \pm \varepsilon(M)$	σ	n	$M \pm \varepsilon(M)$	σ	n	$M \pm \varepsilon(M)$	σ
Illness	18	304.0 ± 40.5	172	19	1.027 ± 0.0017	0.0073	19	578.4 ± 80.2	349.5	19	1.023 ± 0.0016	0.0072
Health	10	574.0		10	1.021		10	801.6		10	1.017	
Individ. diff.: Health, Illness.												
n		$D \pm \varepsilon(D)$	σ	n	$D \pm \varepsilon(D)$	σ	n	$D \pm \varepsilon(D)$	σ	n	$D \pm \varepsilon(D)$	σ
9		+ 171.1 ± 57.8	173	10	0.0073 ± 0.0028	0.0089	10	+ 273.5 ± 102.1	323	10	− 0.0005 ± 0.0021	0.0068

tered ECT. When the serum-iron values were subsequently obtained, it was discovered that he had a value of above 150 gamma per cent when first going to be sent home, and 100 when he was discharged in good health. On being admitted $2\,^1/_2$ years later on account of a new period of depression of a more dysphoric and tense nature accompanied by certain paranoid traits, he had a serum-iron level that was not remarkably high. On the other hand, however, he now revealed a pathologically high and sluggish load curve on receiving iron *i.v.* The depressive component of his clinical picture was more prominent after a few months, accompanied by a rise of serum-iron up to 188 gamma per cent.

Whether the serum-iron level *precedes* the psychic inhibition cannot be ascertained, for a sufficient number of cases has not yet been observed in succession in their free intervals.

In this connection it may, perhaps, be worth mentioning that cases collected from my material, having a remarkably high TIBC, and as a rule, schizoid traits—being of a more malign type—revealed this abnormally high TIBC one or two years before this degeneracy of their clinical picture appeared.

3. Iron tolerance-tests

In cases of depression, intravenous injections of ferrous sulphate in a solution of ascorbic acid were made. Few patients could stand more than 3–7 mg (cf. the high saturation of iron-binding globulin in depressions). Those patients who often suffered from their depression in the mornings, were frequently seized with severe anguish when administered the injections. Some of them even had recurrences of their severe depressive delusions and cardiac angor. In one or two cases, the patient endured the injections relatively well, only manifesting hot and pricking sensations in the head or the legs. At the same time they felt a slight nausea. The curves were high and sluggish as to their return to the normal. The injections were made on fasting patients between 8 to 9 a.m. and administered very carefully, lasting 3 to 5 minutes. In this connection it might be worth mentioning that the patients occasionally possessed a higher serum-iron value at noon than at 8 a.m.

The TIBC of the patients was determined on the morning fasting-values before the injections were administered. Six patients who had, on an average, been given 6 mg of Fe^{++} (4–10 mg), revealed a complete saturation of the TIBC still 6 hours after the injection. The mean value of the serum iron of 5 patients was 190 gamma per cent, 10 hours after the injection.

B. Concerning the Serum Iron of Certain Other Depressive Conditions of a Mixed Type

An investigation was made into the serum iron of conditions of depressive insufficiency, a rather heterogenous group comprising asthenic, exogenous, and depressive mixed states, possibly with presenile traits, and finally into depressive-dysphoric conditions of suspected mild schizophrenia.

Sixteen patients of this type are recorded in Table 27, their individual diagnoses being found in Table 27 B at the end of this book, after the case histories of the main material. They all possess a slight increase of the serum-iron level in comparison with that taken on their admission. Throughout all the cases, asthenic traits, or a certain rigidity, are to be found in these patients, who, in some cases, did not appear to be improved when discharged from the hospital.

As will be seen in Table 27, the serum iron of the patients does not, on the whole, deviate from the normal. Compare the lower value given regarding earlier stages of schizophrenia (Chap. IV).

Ten patients of both sexes having low serum-iron values in the morning (mean value: 74 gamma per cent) mostly had the diagnosis asthenia, or suspected schizophrenia. A few of these are included in the above material of sixteen patients.

The diurnal rhythm of the serum-iron level is considered to reflect the normal biological daily rhythm of the individual. The endogenous depressions of the main material, frequently of a mild form and of a good prognosis with respect to the depression of main interest, manifest somewhat higher values before noon, but otherwise a normal rhythm. Such patients of a mixed type as had an abnormal rhythm with regard to its rise in the afternoons are recorded in Table 28.

Table 27. Patients showing an increase of their serum iron on being discharged from the Clinic. Three men and 13 women.

SI gamma per cent (Morning values)					
At the beginning of the treatments			When discharged from the clinic		
n	$M \pm \varepsilon(M)$	σ	n	$M \pm \varepsilon(M)$	σ
16	121.8 ± 9.9	39.6	16	144.8 ± 8.6	34
Individual differences between the values: $D \pm \varepsilon(D) = -22.9 \pm 8.3$ gamma per cent ($\sigma = 33$)					

Table 28. Patients showing a higher serum-iron value in the evening (inverted curve). Two men and 13 women.

SI gamma per cent		
8 a.m.	Noon	5 p.m.
67.5	104.0	107.5
117.0	146.0	158.5
83.5	99.0	139.0
59.0	62.5	103.5
121.0	119.0	151.0
163.0	151.0	200.0
118.0	176.0	165.0
76.0	140.0	114.0
72.0	83.0	76.0
126.0	141.0	131.0
74.0	85.0	104.0
104.5	135.5	123.0
108.0	104.0	147.0
92.0	82.0	111.0
124.0	183.0	150.0

	n	$M \pm \varepsilon(M)$	σ
8 a.m. . . .	15	101.1 ± 7.6	29
Noon . . .	15	120.8 ± 9.3	36
5 p.m. . . .	15	132.1 ± 8.0	31

Indiv. diff.: morning/evening values

$D \pm \varepsilon(D) = -31.7 \pm 3.8$ gamma per cent ($\sigma = 15$)

As is apparent from the table, these patients show a moderate and significant increase of their serum-iron level in the afternoon. The diagnoses of this series are collected in Table 28 B at the end of this book. As appears from the diagnoses, these patients, too, have preeminently "asthenic" traits, or suspected schizophrenia. In view of the condition of the patients, it was not unusual that anguish, or anxiety, was found in these very individuals towards the end of the afternoon.

The diurnal curve of the serum-iron level was also determined in 9 patients of endogenous depression with regard to the early morning value at 5 a.m. These people suffered from "ordinary" difficulties in sleeping, but in other respects they represented an arbitrary choice.

This value at 5 a.m. was high, approximately the same as the evening value, but 10–20 gamma per cent lower than the 8 a.m. value. A couple of depressed schizoid patients had a higher value at 5 a.m. than at 8 a.m.: Some serum-iron values at 8–9 p.m. revealed a tendency to decrease in relation to the values of 5 p.m.

The *iron-binding capacity* of the serum in some depressive-dysphoric patients with schizoid traits was remarkably high, i.e. more than 400 gamma per cent (a total of 10 cases).

The serum-iron level in cures with soporifics is of certain interest. Blood samples from 5 patients (3 men and 2 women) were daily taken at 8 a.m., noon, and 5 and 12 p.m. Those of 2 individuals were taken 2 days in succession. When tested, each patient had been administered 1/2 g of diemal (diethylmalonyl carbamide) three times a day, as well as 0.20 g of pentymal (isoamylethylmalonyl carbamide), respectively, for at least 6 to 8 days. Their mean curve had the following appearance:

8 a.m.	167
12 noon	174
5 p.m.	171
12 midnight	142

The individual values presented a great spread in these few patients with varying diagnoses.

It is possible that the individual showing the least obvious reaction to soporifics revealed the lowest serum-iron value. The diagnoses of the patients comprised depressive anxiety states. One made an attempt at suicide, one was diagnosed psychopathic, and another was a suspected schizophrene. The latter had the lowest values.

C. Electro-Shock Studies on Endogenous Depression in Conditions of Complete Muscular Relaxation

An investigation was also made, regarding patients with endogenous depression, into the changes of serum iron and haematological data, before and after each individual shock. The results appear from Tables 29 to 34.

As will be seen from Table 31, serum iron does not reveal any remarkable changes prior and immediately subsequent to a single el-shock (the Holmdahl technique was employed). If we regard the changes of the serum iron during the entire series of shocks, there is

Table 29. The serum iron of the patients in the shock series. Values of illness at 8 a.m., noon, and 4 p.m.

	SI gamma per cent
Values in illness 8 a.m. . . .	166.9
Noon . . .	157.2
4 p.m. . . .	127.0
Difference 8 a.m. – noon . . .	9.7
ε (diff.)	12.95
Degrees of freedom	20
t	0.7488
P	$0.40 < P < 0.50$
Difference 8 a.m. – 4 p.m. . .	39.9
ε (diff.)	15.04
Degrees of freedom	19
t	2.6533
P	$0.01 < P < 0.02$

Table 30. Serum iron. Values of illness at 8 a.m. compared with the values immediately after shocks I, II, and III, showing a successive decrease to the normal.

	SI gamma per cent
Morning value, 8 a.m., in illness .	166.9
5–15 min. after el.-shock I . . .	159.3
» » » » II . . .	145.2
» » » » III . .	120.9
Diff. 8 a.m. – after el.-shock I . .	7.6
ε (diff.)	14.8
Degrees of freedom	23
t	0.5135
P	$0.60 < P < 0.70$
Diff. 8 a.m. – after el.-shock II .	21.7
ε (diff.)	18.7
Degrees of freedom	20
t	1.1688
P	$0.20 < P < 0.30$
Diff. 8 a.m. – after el.-shock III .	46.0
ε (diff.)	13.3
Degrees of freedom	19
t	3.4566
P	$0.001 < P < 0.01$

Table 31. Serum iron before and after shocks I, II, and III, showing a level curve during the day of the shock.

The values explain SI in gamma per cent	I el-shock	II el-shock	III el-shock
Immediately before el.-shock	167.9	142.5	125.0
» after »	159.3	145.2	120.9
3 hours after el.-shock . . .	158.2	155.3	136.2
7 hours after » . . .	158.9	137.4	139.3
Diff. before – after el.-shock .	8.6	2.7	4.1
ε (diff.)	13.5	17.9	12.2
Degrees of freedom	28	23	18
t	0.6354	0.1511	0.3348
P	$0.50 < P < 0.60$	$0.80 < P < 0.90$	$0.70 < P < 0.80$
Diff. before – 3 hours after .	9.7	12.8	11.2
ε (diff.)	12.4	17.1	15.1
Degrees of freedom	26	23	16
t	0.7810	0.7476	0.7406
P	$0.40 < P < 0.50$	$0.40 < P < 0.50$	$0.40 < P < 0.50$
Diff. before – 7 hours after .	9.0	5.1	14.3
ε (diff.)	15.6	14.4	14.4
Degrees of freedom	24	22	16
t	0.5788	0.3547	0.9907
P	$0.50 < P < 0.60$	$0.70 < P < 0.80$	$0.30 < P < 0.40$

Table 32. Serum iron, haematocrits, and reticulocytes at various times of the day from patients having recovered after el-shock treatment.

	SI gamma per cent	hct. %	ret. ‰
Values in health, 8 a.m. . .	137.9	43.0	4.6
» » » , noon . . .	133.4	43.2	4.6
» » » , 4 p.m. . .	118.1	42.5	4.3
Difference 8 a.m. – noon . .	4.5	0.2	0
ε (diff.)	9.50	1.32	0.68
Degrees of freedom	15	17	17
t	0.4742	0.1517	–
P	$0.60 < P < 0.70$	$0.80 < P < 0.90$	–
Difference 8 a.m. – 4 p.m. . .	19.8	0.5	0.3
ε (diff.)	8.24	1.40	0.65
Degrees of freedom	14	14	15
t	2.4028	0.3573	0.4647
P	$0.02 < P < 0.05$	$0.70 < P < 0.80$	$0.60 < P < 0.70$

Table 33. Haematocrits before and after shocks I, II, and III. No statistically significant difference during the day of the shock.

The values indicate haematocrits (%)	I el-shock	II el-shock	III el-shock
Imediately before el.-shock	44.5	41.7	41.5
» after »	43.9	41.6	41.3
3 hours after el.-shock	43.6	42.0	43.3
7 hours after »	42.3	42.5	40.4
Diff. before – after el.-shock	0.6	0.1	0.2
ε (diff.)	0.92	1.23	2.15
Degrees of freedom	23	20	16
t	0.6518	0.0810	0.0929
P	$0.50 < P < 0.60$	$0.90 < P$	$0.90 < P$
Diff. before – 3 hours after	0.9	0.3	1.8
ε (diff.)	1.04	1.32	2.10
Degrees of freedom	20	20	15
t	0.8616	0.2281	0.8595
P	$0.30 < P < 0.40$	$0.80 < P < 0.90$	$0.40 > P < 0.50$
Diff. before – 7 hours after	2.2	0.8	1.1
ε (diff.)	1.39	2.10	1.98
Degrees of freedom	19	17	15
t	1.5831	0.3815	0.5590
P	$0.10 < P < 0.20$	$0.70 < P < 0.80$	$0.50 < P < 0.60$

a continuous and successive drop of the serum iron in the direction of the values of health (Table 30). On the day of administering the shock, the evening values were remarkably high, amounting to approximately the same as those of the morning (Table 31).

The shock-series that restored the patients were short, usually comprising only 3 shocks each. Five of the 13–15 patients examined with regard to their diurnal serum-iron curve were administered a fourth shock. Thus, my series reveal an obvious improvement, or a complete remission. The values of health refer to a point of time occurring a week or two subsequent to the improvement.

As to the haematocrits, the immediate increase after the shock is not to be found here (Tables 32 and 33). The reticulocytes did not manifest any remarkable changes. No high reticulocyte counts were observed during the more than forty shocks in more than 160 tests (Table 34).

Table 34. Reticulocytes before and after shocks I, II, and III, showing no remarkably high values, nor any statistically significant differences during the day of the shock.

The values indicate reticulocytes (‰)	I el-chock	II el-chock	III el-chock
Immediately before el.-shock	3.8	3.5	3.7
» after »	3.7	3.8	4.0
3 hours after el.-shock . . .	4.1	4.2	3.9
7 hours after » . . .	3.8	3.4	3.6
Diff. before – after el.-shock .	0.1	0.3	0.3
ε (diff.)	0.46	0.27	0.47
Degrees of freedom	18	19	16
t	0.2182	1.1232	0.6332
P	$0.80 < P < 0.90$	$0.20 < P < 0.30$	$0.50 < P < 0.60$
Diff. before – 3 hours after .	0.3	0.7	0.2
ε (diff.)	0.49	0.30	0.44
Degrees of freedom	14	18	14
t	0.6078	2.3279	0.4576
P	$0.50 < P < 0.60$	$0.02 < P < 0.05$	$0.60 < P < 0.70$
Diff. before – 7 hours after .	0	0.1	0.1
ε (diff.)	0.45	0.30	0.47
Degrees of freedom	15	16	14
t	–	0.3317	0.2142
P	–	$0.70 < P < 0.80$	$0.80 < P < 0.90$

D. Fasting Experiments

Nearly all my tests dealing with the problem of serum-iron changes were carried out together with haematological investigations. In order to obtain an idea of the influence of starvation on serum iron, i.e. the importance of the assimilation activity of the liver, experiments with starvation were made on healthy individuals. In literature there are no results of statistical significance on this point. As I have pointed out in the chapter concerning the metabolism of iron, Jacot had carried out an investigation (on ten patients) proving that serum iron has a tendency to increase during one day of fasting. However, this investigation implied that, besides fasting, the patient was only allowed to drink one glass of water during the experiment period, which consequently assumed the character of stress caused by thirst.

My material comprised 15 individuals. They partook of food in the usual manner the day before fasting. During starvation they were allowed to drink water as they liked. The material consisted of student

Table 35. Serum iron in starvation tests on man.

SI gamma per cent		
8 a.m.	Noon	5 p.m.
146	180	158
182	162	184
62	70	76
84	98	160
190	186	188
100	139	220
98	144	158
121	121	249
105	124	176
147	115	130
107	115	145
140	155	139
157	180	172
124	170	173
135	175	166

	n	$M \pm \varepsilon (M)$	σ
8 a.m. . . .	15	126.5 ± 9.1	35
Noon . . .	15	142.3 ± 8.9	35
5 p.m. . . .	15	165.7 ± 9.8	38

Indiv. diff.: morning/evening values

$D \pm \varepsilon (D) = -39.1 \pm 11.1$ gamma per cent (σ 43)

nurses in their twenties, besides a few male individuals aged about 30. The results are presented in Table 35.

As appears from the table, the serum-iron level of these individuals showed, as a rule, a rise in the afternoon, which is statistically significant, the difference between morning and evening values being -39.1 ± 11.1 gamma per cent.

CHAPTER XI

Discussion of the Results

The aim of my investigations is, *firstly,* to obtain a material of endogenous depressions of the most homogeneous character from a psychiatric point of view. This demands a definition of concepts. Moreover, the problem of differential diagnosis is taken up for detailed discussion, in connection with stressing some diagnostic criteria. The material mainly constitutes cases belonging to *psychiatria minor,* i.e. non-psychotic patients of a depressive type, designated as endogenous depression. They belong to a category which it is possible to treat at neurosis clinics without locked doors. Apart from psychosomatic discomposures, broodings (not seldom psychologically motivated from the patient's point of view), vegetative disturbances, and symptoms from the mucous membranes, the psychomotor inhibition is predominant.

From a somatic standpoint, constitutionally as well as according to the general condition of the patients in the depressive period of main interest, their average status was good. The ordinary laboratory findings indicate normal conditions.

Secondly, as to my laboratory results, the following may be pointed out. During a period of depression, serum iron is remarkably high, especially as far as its morning value is concerned: in men 199.3 ± 11.0 ($\sigma = 43$), in women 169.3 ± 5.8 ($\sigma = 29$). The differences in relation to the normal values, as well as the differences between values of illness and health, are statistically significant. The same is the case with the difference between values of illness and post-examination if the patient is healthy.

In cases where the patient has not recovered, there is no normalization nor drop of the serum-iron value.

The iron-binding capacity of serum is largely to be found within normal limits in endogenous depressions. To a greater extent than usual, the iron-binding globulin is saturated with iron (1/2 in comparison to 1/3 in normal conditions).

A high serum-iron level and a high saturation of the transferrin indicate a transport of iron into the depots (Laurell 1947, Hagberg 1953, Vahlquist *et al.*); compare Chap. III. If the storage occurs in the form of reversible ferritin, or irreversible haemosiderin, this depends most likely on the surplus of iron and the protective colloid obtainable (Granick 1949 and 1951) as well as on the factor of time, i.e. the duration of the depression. In this connection it may be worth mentioning that there is a tendency towards dehydration also in mild depressions, —see my laboratory findings.

The diurnal curve of serum iron—apart from the increase most pronounced in the mornings—revealed a normal diurnal rhythm. The high morning value contradicts the general opinion that calm and undisturbed sleep is a prerequisite of a higher serum-iron value in the mornings. Almost all the patients suffering from endogenous depressions have great difficulties in sleeping—an outstanding trait of their clinical pictures. In spite of this, an abnormally high serum-iron value is manifested in the mornings.

The few *i.v.* iron-tolerance tests made were high, and sluggish in returning to their "normal values", in line with the high saturation of the iron-binding globulin and in conformity with signs of iron intolerance on administering injections.

In depressions of suspected schizophrenics, or in those having "asthenic" traits, the serum iron is rather low. In this group of patients it is not uncommon to find an inverted diurnal serum-iron curve, i.e. one having a higher value in the evenings than in the mornings.

A low morning value in initial states of schizophrenia has earlier been stressed in the literature (see above). My findings concerning schizoid-depressive states speak in favour of this fact.

The iron-binding capacity of these conditions is obviously high in my material (TIBC $>$ 400 gamma per cent).

In man there is a significant increase of serum iron during starvation (with a free intake of water). As to this increase, it may be pointed out that Jacot found that rest in bed during the day of starvation lowered the tendency for an increase of serum iron, whereas motor activity and work increased the serum-iron level. The diminished activity found in patients having endogenous depressions may therefore, *per se,* hardly influence the serum-iron level as an increasing factor. Any activity by the patients (including a forced one) might, on the other hand, bring about an increase of this level.

Experiments with rabbits treated with ECT ("subjects in normal conditions") possibly speak in favour of an increased erythropoiesis (e.g. an increase of the reticulocytes), and further in favour of a slight tendency for the serum-iron level to increase after the completion of the series. The latter phenomenon is exactly the reverse of what is the case with regard to endogenous depressions.

From a haematological point of view (hb., Er., ret.), endogenous depressions show values within normal limits. The same is the case with other conditions discussed here. Further, their haematocrit values, their plasma volume, as well as their total serum protein, were also normal.

My findings confirm earlier investigations in this latter respect. The slight tendency towards an increase of the haemoglobin value, the number of erythrocytes, and that of the reticulocytes during the improvement of the patients point to a decreased erythropoiesis in the de-

pressive state. The high serum iron level during infirmity might possibly speak in favour of a somewhat inferior haemoglobin synthesis in illness and a lowered capacity for utilizing iron.

With regard to the *sympathetic adreno-cortical system,* often discussed in connexion with ECT, mention may be made of the important position of adrenals as a factor in the control of the serum-iron level (Cartwright *et al.,* 1949—1950, experiments on dogs and rats). Paterson *et al.* (1952) stressed the fact that ACTH and cortisone do not influence the diurnal variation in the serum iron level in man.

The fact that ACTH and cortisone do not act specifically in the treatment of endogenous depression does not support the assertion that deficiency of these hormones is of significance in the aetiology of this state of disease (Altschule *et al.* 1950). A lack of ACTH and cortisone can thus hardly be considered to be the *primary* cause of the changed serum iron level in endogenous depression.

On the other hand, such an indirect adreno-cortical influence can hardly be excluded. Compare the tendency found, which speaks for a changed water-metabolism in endogenous depression.

The effect of ECT on the sympathetic adreno-cortical system is, amongst others, discussed by Sälde (1952). The leucocyte changes in endogenous depression after shock were not recorded as deviating from those obtained in other depressive mixed conditions. Endogenous depression manifested the same stress-response as these conditions, thus depriving endogenous depression of any unique position in this respect.

It is generally agreed that increased activity within the *reticulo-endothelial system* results in a fall of the serum-iron level. The high serum iron in endogenous depression would thus appear to indicate reduced activity or relative insufficiency within this system.

The influence of the *liver* upon the serum-iron level is stressed by the author. The investigations made, starvation experiments in man, suggest that the assimilation of food constitutes an essential condition for the fall in serum iron which normally takes place during the course of the day. (Cf. the often inverted diurnal curves—the serum iron increasing, towards evening, in depressive states with schizoid traits, which might possibly suggest disturbance in the assimilatory processes.)

It should here be recalled that Chemnitz (1952) found signs of liver damage in 12 of 16 patients with manic-depressive psychosis (degree of severity not specified) by means of Felix's Test – acid test, at the same time reviewing some earlier investigations into this field. Further it may be mentioned that Hult's findings (1950) of transient states of psychic insufficiency accompanied by fatigue and moodiness and incapacity for work were correlated with fatty degeneration of the liver, which disappeared on the patient's recovery. The changing state of the liver was successively followed by means of biopsy.[1]

[1] A general discussion regarding hepatic disorders in mental derangements is not

The altered values of serum iron in depressive states probably have a complex origin. The important question as to the nature of the conditions seems to be bound up with the very metabolism of the cells of the organism.

Practical clinical viewpoints. In depressive states, a high serum iron speaks for endogenous depression and for an expected positive effect of electro-shock treatment. A high serum iron remaining after treating the patient contradicts the cure of the morbid process.

A reversed diurnal rhythm, i.e. a higher serum iron in the afternoon than in the morning in depressive conditions—possibly in connection with an obviously low morning value—argues for a more pronounced disturbance of the biological equilibrium of the patient. A reversed diurnal rhythm of the serum-iron level has been found in depressions of suspected schizophrenia and in highly "asthenic" depressions.

discussed here, nor influence of liver diseases on the serum iron. The clinical investigations of the liver function in mental maladies usually deal with cases of the *psychiatria major* type, and are thus not relevant in this connection.

CHAPTER XII

Case Histories

Men

Case 1. 648/51, age 54. Farmer. Married.

Hered. No definite heredity as to psychic maladies.

Somat. Diseases. On the whole healthy. Contracted the mumps in June, 1937.

Somat. Findings in Oct., 1951: Pyknic type. Height 161 cm, weight 70 kg. Cor 0. Blood-pressure 130/100. Otherwise nothing noteworthy somatically and neurologically. (Somewhat fumbling movements.)

Psych. Premorbid personality. Debile. No detailed information could be obtained concerning his premorbid personality, but he is a little hot-tempered. Not suspicious, nor agressive.

Case History. Nothing noteworthy during childhood and adolescence. Completed his elementary education and was confirmed. In 1931 he took over his paternal farm, which he has managed since then. Married in 1930. His marital relationship is said to be good. Three children living. The first period of depression occurred in 1937, when he was nursed at Ulleråker Mental Hospital for a depressive psychosis of a manic-depressive type. After two months at the hospital he was sent home in the middle of Oct. As a releasing factor there may be mentioned the patient's mumps in the summer of 1937. He was careless with this malady and went on working during his illness. There were initially a few suicide attempts during this period. His next depression came in 1947, when he was nursed at the Clinic for about a month in the middle of the summer on account of a manic-depressive psychosis. He was depressive, somewhat dull of mind, having strong delusions of sin and self-reproach, and woke up early in the morning brooding. The period of illness had lasted several months before his admittance, i.e. from the spring of 1947. Recovered after ECT (5 shocks). A third period of the same type was cured with ECT at a mental hospital in Sept., 1949. In good condition on being discharged. The period of chief interest occurred in the autumn of 1951, when the patient was nursed for a manic-depressive psychosis at the Clinic during the latter half of October. (Oligophrenia was observed then, as well as on his previous admittance to the Clinic.) This period started in the middle of Sept. with sleeplessness, which soon assumed the character of an endogenous rhythm accompanied with anxiety in the small hours. His mornings, worse. Dryness of the mucous membranes and constipation, but no remarkable loss of weight. Recovered after ECT (5 shocks). When admitted to the hospital he was frustrated, anxious, and also somewhat irresolute; but there was no foundation for a schizophrenic process, and he had fully recovered when discharged.— A new period occurred in the autumn of 1952 with the same picture of inhibition depression, delusions of sin, and sometimes of agitation—this time too with a typical endogenous rhythm. Treated with 5 el-shocks. Was in a rather good condition when discharged in the middle of Dec., but relapsed a little into his depression in Jan., 1953, on account of which he was given an additional 4 el-shocks. After these he was cured, and, when discharged in Jan., he was calm, cheerful, and optimistic.

Post-examination by letter in March, 1954. The patient claims to be in good health, having good sleep and a good appetite. No complaints of discomfort.

Case 2. 345/51, age 51. A former cattleman. Married.

Hered. No sure heredity with respect to nervous diseases. 1/8 brothers and sisters. At least one brother has periodical nervous troubles of partly the same character as those of the patient. Further, a few of his brothers and sisters have a "nervous" disposition.

Somat. Diseases. Was nursed at Nynäs Health Resort in 1932 and 1933 for V.O.C. and a neurosis, a diagnosis that was made during his last period of treatment there. Gastric ulcer suspected in Dec. 1932, confirmed in 1953. No operation. Moreover he was afflicted by muscle pains, probably of a psychosomatic nature. Was nursed for a suspected infarctus cordis in 1950.

Somat. Findings, June 1951: Pyknic type. Height 168 cm, weight 73 kg. Cor: no signs of incompensation, physically normal findings. Blood-pressure 180/95. Otherwise nothing noteworthy from a somatical point of view. ECG normalized (no signs of infarct as above, 1950).

Psych. Premorbid personality. The patient managed quite well at school, being probably intellectually normal. Perhaps somewhat pedantic, but without any neurotic, obsessive, or compulsive reactions. Was relatively well adapted to his situation, and generally got on well at the places he worked. When healthy, he was industrious and efficient with a certain tendency towards uneasiness during autumn and spring. Uses alcohol moderately.

Military Data: Completed his training without remarks, as well as his extra compulsory service.

Case History. Healthy as a child. Good connections in his parental home. No disturbances until adolescence (recorded below). Married in 1924. Three children, now married, are not quite strong. His wife is somewhat infirm, but she manages her home without any difficulty, which is also confirmed by her neighbours and relatives. No matrimonial nor sexual problems. No economic troubles.

At the age of 17 there was a period of infirmity during 3 months with a sensation of weakness in his legs without any simultaneously infectious or febrile reaction. A second attack at the age of 22, lasting for a fortnight. At this time too, he was, on the whole, incapable of walking. Moreover, the conditions accompanying the attacks are not quite clear. In 1932 and 1933 he was nursed at the Nynäshamn Health Resort for his nerves, his diagnosis during the last time being mitral insufficiency + a neurosis.

No heart troubles, and quite vital and capable of working afterwards, apart from his autumn and spring periods, and during the illness of chief interest. Grew worse in 1944, or 1945. Used to be quite healthy during summers. His periodical troubles manifested themselves above all in psychosomatic gastro-intestinal disturbances and angor of the chest, and during recent years predominatingly over the heart. At the same time there were difficulties in sleeping, mostly in falling asleep. During later years there appeared a depressive component in the picture. His condition was somewhat fluctuating from day to day and used to disappear gradually after a month or two. In the late autumn and before the Christmas of 1949 the angor over his heart increased, changing character, and he was also afflicted with cardiac anxiety of a different kind than earlier. Was nursed in Jan. and Febr. 1950 for a probable infarctus cordis.

A further degeneration during the spring of 1951—the period of main interest —caused his admittance into the Psychiatric Clinic in June. He was depressive, lost weight in connection with his illness, more than 10 kg, having polysymtomatic troubles of a psychosomatic character with dizziness and buzzings in his ears; was somewhat lachrymose and found it difficult to concentrate. With a view to his depressive picture, he was given el-treatment (3 absences and 3 shocks) after a sedative insulin treatment. After about 2 months he was discharged on August 11, with opium as a home-treatment, and was controlled policlinically. Grew worse in the autumn and had to be admitted again into the Clinic in Nov., when it

was observed that his old disturbances had returned. He was uneasy and anxious. Lost his appetite and had reduced about 4 kg since his discharge. His spirits were far below the level, he brooded on his future, but there were no real depressive delusions. In spite of a certain improvement in Dec. a pension for illness was considered advisable, and on account of his heart it was thought better to refrain from an exacting therapy.

Post-examination in March 1954: The patient's condition is about the same as prior to his admittance into the Clinic, and he draws a pension for illness, which has been prolonged after his period of treatment at the Clinic in the autumn of 1952. His periodical inconveniences in the autumn and spring have returned, manifesting themselves late in the autumn of 1953 in the form of ulcus disturbances, and he was taken to a hospital from Dec. 1953 to Jan. 1954 for an ulcus ventriculi (malaena). No operation.

Case 3. 739/51, age 48. Forester. Unmarried.

Hered. A paternal uncle treated at a mental hospital, now recovered. 2/2 brothers, the elder being healthy.

Somat. Diseases. Claimed very good health, never ill.

Somat. Findings in November, 1951: Pyknic-athletic type. Height 168 cm, weight 78 kg. Cor o. Somat. and neurologically normal findings.

Psych. Premorbid personality. Normally gifted. Was always extrovert. Easy to establish contacts and get along with strangers. Not tense, nor unconfident in himself. Morning-active. Adapted to his duties. No asthenic traits. Spring fatigue during mature age. Military training and extra service without remarks.

Case History. Normal development. Engaged in forestry since youth. Led a somewhat vagrant life. Several contacts with the opposite sex without marriage. Liked his work, and was generally in possession of good working-capacity.—First depression period in the autumn of 1932. Had feelings of inferiority and felt superfluous, being at the same time inclined to weeping. This period was over after a month or two. Unemployed on this occasion.—The second depression period set in during the early spring of 1951. He consulted a psychiatrist in the middle of February, grew worse, and was admitted into the Clinic at the end of April. Felt tired and exhausted, depressed, and found it difficult to sleep (zerhackter Schlaf). Had feelings of self-reproach on account of his having to be a witness at some legal proceedings. Numb feelings in his hands and vegetative uneasiness accompanied with sweating and palpitations of the heart. A moderate inhibition was observed, but no noticeable depression besides that. His depression was, to a certain extent, regarded as released. After being treated with sedative insulin and hormones, the patient was discharged in the beginning of June. Was not quite restored during the summer and grew worse during the autumn. He was now afflicted with a more pronounced depression—the period of main interest. Found it difficult to get started in the mornings, being incapable of rising until after noon. Had not been able to resume his work since early spring. Had a parched throat. Brooded on the past. Endogenous diurnal rhythm as well as an incapacity for sleeping in the early hours. Moreover, his clinical picture was reminiscent of the one in the spring, there being only a moderate inhibition. ECT was regarded as necessary. Four shocks yielded very good results, and the patient was discharged in good health on Dec. 21st.—With a view to obtaining a health certificate for official service, owing to a change in his office, he was re-examined in the autumn of 1952 at the Clinic, and good health was ascertained. The patient claimed that the previous shocks had changed him completely for the better. Now there was no depressive picture left. His optimism in work returned. His memory was good, as well as his working capacity.

Post-examination in March, 1954: The patient was certified as possessing full health. No depressive thought. His appetite and sleep were good.

Case 4. 753/51, age 44. Official, married.

Hered. His father died of a heart disease. His mother had a few depressive periods and was nursed at a mental hospital on one occasion; died of a cerebral haemorrhage at the age of 68. 2/3 brothers and sisters. An elder brother died as an infant, a younger sister is healthy.

Somat. Diseases. On the whole in good physical health.

Somat. Findings, Dec. 1951: Pyknic type. Height 170 cm, weight 79 kg. Cor 0. Blood-pressure 130/90. Otherwise normal conditions somatically.

Psych. Intellectually well endowed. University education. Of an even temperament, and usually of a cheerful disposition; good working capacity. Not unconfident in himself nor easily offended, nor vulnerable; not asthenic. Besides a rather considerable amount of work, he has sufficient vitality for hobbies. Syntonic traits with an obvious tendency towards gloominess, particularly in the autumn.

Military Data. Nothing noteworthy.

Case History. Parents' home good. No maladjustment as a child, nor during adolescence. Good results at school. Got on well with teachers and students, establishing good contacts among them.—The first mild depression occurred in 1926 at the age of 19. In 1933, the next one came, and he was treated at a mental hospital in the spring of that year under the diagnosis of manic-depressive psychosis. He had studied very hard and had also got entangled with a girl before he became ill. A third and somewhat severer depression in the spring of 1934 caused him to be admitted again into a mental hospital for a period of about 4 months. He was frustrated, apathetic, complaining that he was emotionally dead, and of the definite opinion that he was afflicted with schizophrenia. In April 1937 his fourth depressive period set in, preceded by fatigue and difficulties in sleeping. This time there was a slight dazed state of mind initially, and a certain feeling of catastrophe. This period gradually ended towards the summer. No disintegration, nor any schizophrenic symptoms were observed during his stay at the hospital. During the next few years he was healthy and capable of working—on one or two occasions possibly slightly hypomanic—but otherwise well adapted. Good connection in marriage. One daughter, healthy.

A fifth depression, that of chief interest, occurred in the autumn of 1950 with difficulties in sleeping—at times with an endogenous rhythm of sleep. Despondent, anxious (especially in the morning): started brooding, and became tired and indifferent. On this occasion his working conditions and night service were very exacting. Grew worse and incapable of working in the spring of 1951, and applied for admittance into the Psychiatric Clinic, where he was accepted in June. His picture was that of a psycho-motor inhibition, being at the same time anxious, tense, and perhaps somewhat irresolute. No hallucinations nor delusions. No schizophrenic symptoms. On given ECT (4 el-shocks), he was discharged as improved at the end of July after a slight hypomanic reaction. Again admitted into the Clinic in Dec. 1951, as he was not fully restored. Could not get started in the mornings, not feeling normal until noon. Unconfident in himself and frustrated when he arrived—the same clinical picture as in July. ECT (4 shocks) gave a good result. His self-confidence returned and the inhibition disappeared. Was discharged in a sound condition on Febr. 14. After being discharged he was capable of working and healthy, was able to manage a responsible position and was found to be recovered on his post-examination in March 1954.

Case 5. 40/52, age 46. Farmer. Unmarried.

Hered. His father, a farmer, committed suicide during a depressive period at the age of 49. One brother did the same in his thirties. 3/6 brothers and sisters, who are healthy.

Somat. Diseases. Healthy, apart from "sensitive air-passages" in the winter;

from the age of 30 he suffered periodically from lumbago. Furthermore he had an accident in 1938, when he was trampled by a horse: Fractura costarum 4–7 dxt laesio pulmonis cum emphysemate subcutaneo. Fully recovered afterwards. No injury of the head.

Somat. Findings in Jan., 1952: Undecided leptomorphic type. Height 173 cm, weight 70 kg. Cor o. Blood-pressure 140/90. An X-ray of the lungs revealed signs of a cured pleuritis on the right side, but otherwise normal findings. Spinal column: slight arthrosis deformans changes of the thoracic and lumbar regions.

Psych. Intellect normal. He is usually an industrious and efficient farmer. Used to be cheerful, even-tempered, extrovert, and finds it easy to agree with people. During maturity somewhat depressed and melancholy in the autumn (Nov.), and in the spring before leafing.

Military Data. Nothing noteworthy.

Case History. No maladjustments as a child. Had a good parental home. Was at the age for conscription when his father committed suicide. Earlier he had several girls, but no marriage resulted. He took over the farm, about 90 acres, which he managed largely himself. He lived with his mother and an unmarried sister. His other brothers and sisters are married and socially well adapted. Felt at home as a farmer, and as a conscript during his military service; got on well with people, etc., but he had periodical troubles as above. The first pronounced depression appeared in the spring of 1951. He became anxious, finding it difficult to sleep, brooding and worrying over the harvest and the purchase of a tractor. Improved in the summer of 1951, but grew worse in Nov. Again difficulties in sleeping, initially not being able to fall asleep. Pains and pressure on the chest. Hypochondriac and anxious, thinking he had tuberculosis and heart disease. He consulted a doctor, amongst others, and had himself examined at a sanatorium. Psycho-motor inhibition and no initiative. Pronounced suicidal intentions. Wanted to go to the woods and kill himself. "Everything is hopeless and so dark." Symptoms of the mucous membranes: "Dry and stiff of the eyes and a parched mouth." His farm-hand quit his job in the autumn, and he began to brood on having to carry out his work alone on the farm, thinking he could not afford to employ a new worker.—He was admitted into the Clinic in Jan., 1952, as an acute case on account of the imminent risk of suicide. He manifested a moderate endogenous depression, being somewhat tense, possibly epileptoid. His sleep was satisfactory. There were no signs of disintegration, obsessive symptoms, nor paranoid traits. ECT (5 shocks) gave very good results. He put on weight, 3 kg in 3 weeks. Was discharged as improved on Febr. 5.

After his discharge, the pains in his back remained, partly in the form of sciatica, during the spring and autumn of 1952, and occasionally also in the spring of 1953; but his hypochondriac ideas and suicidal thoughts had disappeared. Fully recovered after the summer of 1953.

Post-examination in March, 1954: The patient claimed good health and working ability. He was syntonic and accessible, being on a normal level, and did not show any rigidness. The assumed epileptoid trait was not to be found. His weight was constant, and his sleep and appetite satisfactory.

Case 6. 82/51, age 57. Fisherman. Married.

Hered. No definite heredity as to psychic diseases. His mother perished by drowning when the patient was 8 years old—not supposed to be suicide.

Somat. Diseases. Periodical gastro-intestinal disturbances, especially in the autumns, since 1936. Ulcus duodeni in 1948. Gall-bladder operation in the autumn of 1951. No complications. No jaundice.

Somat. Findings on Jan. 31, 1952: Pyknic type. Height 175 cm, weight 68 kg. Cor o. Blood-pressure 130/80. A scar from a gall-bladder operation on his abdo-

men. The urobilin and urobilinogen of his urine was negative, as well as other hepatic tests. Otherwise somatically normal findings.

Psych. Premorbid personality. Normal intellect. Claimed by his wife to be a warm-hearted husband and father with a feeling of responsibility. Gloomy at times, but mostly of a humorous turn. Active and vital. Did not break down, in spite of the fact that his home had been sacked three times by the Russians. Enterprising and adaptable, having no asthenic traits, but somewhat hot-tempered. Autumnal depressions for several years during maturity.

Military Data. See below.

Case History. Nothing noteworthy during the years of his childhood and adolescence. Participated in the Finnish Civil War on the side of the Whites, at the age of 22. Went to sea in his early youth. He also tried to make a living as a carpenter in Australia. He fled from the Russians in 1940 (Esthonian Swede) and obtained Swedish citizenship in due time, after which he settled down as a boat-builder and fisherman in the district of Roslagen. Married at the age of 22. His wife is healthy, and so are his two sons, who are grown up and well adapted socially. Marriage harmonious. No economic troubles. In spite of external difficulties, he always managed to adapt himself. His autumnal periods with gastro-intestinal disturbances assumed a more depressive character and grew worse.

After a gall-bladder operation, as above, he suffered from lack of sleep and a concomitant endogenous diurnal rhythm, became tired and lacked initiative, brooding in the morning, but was almost normal in the afternoon. Dry of mouth. Wanted to cry but could not. Grew worse late in the autumn and towards the Christmas of 1951. On being admitted to the Clinic on Jan. 31, 1952, his picture was that of an endogenous depression having the above symptoms and an obvious diurnal rhythm. Difficulties in sleeping of the type "zerhackter Schlaf". He kept on reproaching himself, mostly for making one of his sons choose the wrong profession, which was in reality a rather good choice. His condition remained the same during his treatment with sedative insulin; but his improvement was obvious after ECT (5 shocks). His sleep returned, and he became more cheerful. His syntonic constitution came to the fore. Was discharged in a rather good condition on March 12, 1952. After this he was not quite capable of working, and towards the autumn his depressive picture returned. Was admitted in Nov. 1952 on account of a pronounced inhibition depression with a certain dullness of mind and vague olfactory hallucinations. At the same time, he was to a certain degree suspicious and uneasy. No splitting nor foundations for schizophrenia. Improved on ECT when discharged in Dec. Renewed depressive reaction in the spring of 1953. And the patient's refusal of further therapeutic tests as well as his general condition resulted in his obtaining a pension for illness on a temporary basis.

Post-examination in March, 1954: A moderate dysphoric depressive reaction was confirmed, and the patient did not feel capable of working. Claimed difficulties in sleeping and could only do easy work to a small extent. His pension for illness was renewed.

Case 7. 178/53, age 47. Farmer. Married.

Hered. No manifest heredity for mental diseases. 7/8 brothers and sisters, one brother having died from rheumatic arthritis.

Somat. Diseases. On the whole, healthy.

Somat. Findings in March, 1953: Undecided athletic type. Height 172 cm, weight 72 kg. Cor 0. Blood-pressure 135/90. Moreover, normal somat. findings. (X-ray: healed fracture of the left scapula).

Psych. Intellectually well endowed. Industrious and is able to manage his farm without any difficulty. Well adapted to his social position. A fiduciary in his native locality. When healthy, he is not timid nor vulnerable. No asthenic traits. In maturity he was somewhat depressed in the autumns, being a little moody.

Military Data. Training without remarks. A released depression period during extra compulsory service in 1943, there being no complications during his first conscription 1940.

Case History. No neurolability as a child nor during puberty. From his youth he was a farmer, and was fond of his occupation. Married in 1936. His wife healthy, as well as his two children. Good marital relationship. His first depression period appeared at the age of 37 when carrying out his above military service. As releasing factors there may be adduced an infection and his changing from one farm to another. Was exempted from military service, but grew depressed, uneasy, and sleepless. Had to be taken into a mental hospital in the autumn of 1944 for a period of six months. He was treated with insulin and shocks, having the above scapula fracture as a complication, as well as some ruptures of the muscles.—In Nov. 1952 his second depression period—the one of chief interest—set in. Began to brood and became incapable of doing work, showing an endogenous diurnal rhythm. Woke up during the small hours in anguish, reproaching himself. Only sat idle in the forenoon, his body feeling as heavy as lead. No releasing factors this time. Was received at the Clinic in March, 1953, because he did not improve. When examined, he was gloomy and depressed, and the endogenous traits of his depression were confirmed. El-shock treatment was considered necessary. After 4 shocks (with total relaxation of the muscles) he recovered completely. When discharged in the middle of April 1953, he was without any inhibition. Happy, open-hearted, and accessible—quite a different person than before.

Post-examination in March 1954: Quite healthy. Manages his work easily. Sleep and appetite satisfactory. No depressive thoughts any more. Accessible and without any psychic rigidness.

Case 8. 223/53, age 65. Labourer. Widower.

Hered. His mother was periodically depressed. One son suffered from periodical heart neurosis of the autumnal and vernal type. 8/9 brothers and sisters.

Somat. Diseases. In 1922 haematemisis, which recurred in 1925 and 1930. His gastro-intestinal disturbances always appeared in connection with a depression, and were generally preceded by some kind of infection of the upper air-passages.

Somat. Findings, March 1953: Pyknic type. Height 165 cm, weight 83 kg. Cor 0. Blood-pressure 180/90. A general slowing and loss of freedom of movement, which was a little jerky and accompanied by slight rigidity and tremor of the fingers as well as the "cog-wheel phenomenon". Otherwise nothing noteworthy from a neurological viewpoint. Achylia gastrica.

Psych. The patient gives the impression of a predominantly syntonic constitution with a normal intellect. He has a pronounced tendency towards periodical moodiness often in connection with gastro-intestinal disturbances. In recent years there was a certain lachrymosity. When healthy, he was industrious, vital, and morning-active.

Case History. Parents' home good. No maladjustments during childhood or adolescence. Married in 1913. His wife died in 1933 of pneumonia. 5 children, on the whole healthy. However, one is nervous, suffering periodically, as above. The patient's constantly recurrent depressions necessitated psychiatric treatment for the first time in 1949. They generally started with irritation, fretting, and fatigue; then uneasiness, anxiety, and brooding. He used to harbour notions of inferiority and suicidal intentions. He was slow and frustrated, had poor sleep of a pre-eminently endogenous rhythm; between times he would be hypomanic and strained. Was nursed for an endogenous depression of a diurnally rhythmic type, symptoms of the mucous membranes and an endogenous rhythm of sleep during April–May 1949; and further a second time during Sept.–Dec. of that year. Was treated with el-shocks and insulin, and discharged in good condition in Dec.

The depression of chief interest started late in the autumn of 1952 and had a

typically endogenous character. He was depressive, having pronounced delusions of sin and inferiority, as well as vague suicidal intentions. On his admittance into the Clinic on March 30, 1953, certain aspects of his picture revealed agitation. After 5 el-shocks and subsequent treatments with histamine and suxil for 14 days, the patient was discharged in a good condition on April 30 after a month's stay at the Clinic.

Post-examination by letter in March, 1954: The patient revealed comparatively good health, but claimed to have certain gastro-intestinal disturbances.

Case 9. 244/53, age 51. Barber. Married.

Hered. His mother was nervous. Otherwise, no hereditary mental disorders. 2/9 brothers and sisters, one brother having eczema and being a little nervous.

Somat. Diseases. Healthy.

Somat. Findings in April, 1953: Pyknic type. Height 173 cm, weight 80 kg. Cor 0. Otherwise somat. nil.

Psych. Premorbid personality. Intellectually normal. Industrious and clever. Able to get started in the mornings. Independent business (ladies' hairdresser). Somewhat sensitive and timid, and possibly a little pedantic, but is well adapted to his work and social standing. A tendency to moodiness, especially in the spring during at least the last 6 to 8 years.

Military Data. See below.

Case History. Somewhat feeble as a child, and a little late in developing. Walked in his sleep for some time, but otherwise did not show any maladjustments or neurolability. After serving in the Navy for seven years, he definitely took up his work as a barber. An active athlete in various fields. Married 1929. Good marital connection in spite of losing his only child immediately after its birth. —The first depression period occurred in the early spring of 1933 when he was 31. Found it difficult to sleep in the small hours, and woke up brooding. Could hardly manage his work. The period died down after a few months. Probably lost a little weight.

The period of main interest appeared in February 1953. Thought he had contracted a venereal disease, a delusion he could not get rid of in spite of proofs showing the contrary. Grew worse and remained in bed without being able to get up and work. Brooding on his hypochondriac ideas. Could not sleep, especially in the small hours, Was depressive, reproaching himself often. No feelings of being offended nor counteracted and thwarted. His condition necessitated his admittance into the Clinic, where his anamnesis was confirmed. He was brooding, but preponderantly tense and anxious. Lost 6 kg of weight during this period of infirmity. His appetite was poor, and he felt dry of mouth. Improvement after 3 el-shocks. Discharged in May 1953. However, he was now not fully recovered, suffering from an insufficiency of the back, which was also confirmed by surgeons. Tense, anxious and brooding, and not able to get rid of his hypochondriac ideas. Improved during the last half of the summer, but grew worse in the autumn, and was again admitted into the Clinic in the middle of November. The same picture as before, but the secondary neurotization was more pronounced. The endogenous component of his clinical picture was primarily taken into account. An initial histamine treatment was administered, whereupon he was given 3 el-shocks. Discharged in a good condition on the 1st of Dec.

Post-examination in March, 1954: The patient is now healthy and capable of working. His optimism has returned, and he has now got rid of his hypochondriac delusion and broodings. Is sociable, open-hearted, showing no rigidness.

Case 10. 241/53, age 21. Shop assistant. Unmarried.

Hered. His grandfather was treated at a mental hospital on account of an endogenous depression with paranoid traits during middle age. Also a paternal

uncle was nursed at a mental hospital. The patient's parents were in good health. His father is a merchant. 1/2 brothers, his brother being healthy.

Somat. Diseases. Delivered by forceps, yet without particular complications. Mumps without cerebral symptoms during the summer of 1951. Febrile for a week. Otherwise of good health.

Somat. Findings, April 1953: Leptomorphic type. Has a comparatively gracile skeleton. Rosy complexion (cf. his age). Height: 183 cm, weight: 67 kg. It was observed that his hands were somewhat damp and warm, not revealing acrocyanosis nor coldness as is usually the case with asthenic depressions. Cor o. Blood-pressure 140/70. Besides this, nothing of somat. interest. EEG: normal findings? (Curve not satisfactorily organised).

Psych. Intellectually well endowed. Clever at school. Intermediate matriculation examination. Industrious and tenacious. Possibly somewhat pedantic. When sound he had no asthenic traits. Had been employed in his father's shop, being able to keep track of everything and recognizing everybody. Perhaps somewhat of a retiring disposition, but enjoys fellowship with friends. Likes dancing.

Military Data. See below.

Case History. Good childhood home and relation to his parents. Pleasant and kind as a child. No anorexia. Occasionally bit his nails, and was a little afraid of the dark. Got along well with his teachers and his school-mates. His first period of depression occurred in the spring of 1950 when he was 18 years of age. He had previously, at Easter-time of the same year, suffered from a cold. Became depressed, anxious. His work proceeded slowly, and he could not get started properly. On one or two occasions he had an indefinite feeling of catastrophe. He went to the Psychiatric Policlinic, having a good insight into his malady. There were no signs of schizophrenia, and he was completely restored after a few weeks of rest in his home. In the middle of October, 1951, there started a new period of depression; he felt tired, indisposed, and without initiative, being at the same time somewhat irresolute. A certain endogenous diurnal rhythm was confirmed with an increase of the symptoms of his malady in the morning, and his symptoms were about the same as during his first depression. Restored after a short period of treatment at home. Was regarded fit for military service, most of which he did in the spring of 1953. Felt quite well until the last week of March of that year, when a new spring depression set in. Grew depressed, uneasy, brooding, suffering from an inferiority complex and vague delusions of sin, accompanied by difficulties in sleeping—yet not of the morning type. Was admitted to the Clinic in April, 1953. Even now, no schizophrenic symptoms were to be observed. A certain endogenous diurnal rhythm was manifest. The patient was treated with insulin in a sedative dose, vitamins and Doca without any correction of his depression. After a couple of el-shocks the depression vanished. His spirits became more cheerful, his confidence returned as well as his optimism. Was discharged in good health at the end of May, 1953.

Post-examination in March, 1954: The patient was healthy, sociable, not showing any psychic rigidness. He was emotionally pliable. His memory and working capacity were good. No difficulty in remembering, e.g. the prices of various articles in the shop. Was able to work from 8 a.m. to 6 p.m. Interested in hobbies and the other sex. His weight was constant, and his appetite good. However, he suffered from a slight depressive reaction in the beginning of the year, including principally certain difficulties in sleeping in the small hours and indisposition in the morning, but was restored after two el-shocks policlinically.

Case 11. 264/53, age 54. Gardener.

Hered. His father, an alcoholist, committed suicide during a depressive period at the age of sixty. Mother sound and healthy. 6/10 brothers and sisters, two of whom died as infants, the remaining seven being healthy.

Somat. Diseases. Slight attack of the Spanish flu during his military service. Not confined to bed. Hepatitis epidemica in 1947, also slight and without hospitalization.

Somat. Findings, April 1953: Undesignated type, possibly having some athletic traits. Height 175 cm, weight 75 kg. Somatic findings: nothing noteworthy, except an S-shaped scoliosis and a disc degeneration below Th XII in the X-ray film.

Psych. Intellectually mature. When healthy, industrious and extrovert. Independent occupation. Liked and appreciated. Trusted member of the community, being for instance chairman of the Board of Child Welfare. Reveals a predominance of syntonic traits, having a tendency to being depressed.

Military Data. Nothing noteworthy.

Case History. No maladjustment during childhood or adolescence. Married at the age of 30. His wife of a cheerful nature and healthy, except for a tendency to rheumatic reactions, not of a severe type. No marital disturbances, and also assisted by his wife in gardening. Two healthy sons. No exogenic troubles nor conflicts.--First depressive reaction in his late teens. Went to see a doctor on account of a pressure on the chest and difficulties in breathing. A second depressive period at the age of 27, accompanied by some psychosomatic disorders and in conjunction with a slight accident without any injury of the head. Recurrent mild depressive periods in the autumn or spring, with intervals of 5–6 years and lasting for about a month. First contacted the Psychiatric Clinic in the autumn of 1948, his malady being designated an endogenous depression. Treated policlinically, recovering during the winter. An increasing depression starting in March 1949 required treatment in the psychiatric ward in May. An endogenous diurnal rhythm was confirmed. Poor appetite. Anguish in the mornings. Easily tired and incapable of work even after nights of some sleep: "Everything is so hard to do." Recovered in May after ECT, 5 shocks.—A new depression of a frustration type occurred in the autumn of 1950, and the patient was treated at the Clinic for a couple of weeks in the beginning of December of the same year. A depression not so severe, but having a pronounced diurnal rhythm, was confirmed. A slight angor of the heart: "I can feel my heart, and I grow uneasy." A slight loss of weight in connection with this depression. Recovered after ECT, 3 shocks.

The depression of main interest began in the early spring of 1953. It was as severe as that of 1949. The patient was nursed at the Clinic during April 16–29. Loss of appetite and a few kg of weight. He suffered from inferiority complexes and, in addition, manifested signs of a moderately frustrated endogenous depression having a noticeable diurnal rhythm. Completely recovered after three el-shocks. Sound and capable of working up to New Year 1954, when he had a new depression of the usual type. He suffered then from inhibition and a total incapacity for carrying out any work, brooding on his father's suicide and his own malady and melancholia. Once more cured by ECT. Sent home restored after a few weeks.

Post-examination in March, 1954: The patient felt quite well and was sociable. Sleep and appetite good as well as his capacity for working. On being examined, he revealed syntonic traits without any rigidness nor levelling down of personality. Had the same feelings for his family and occupation as before, and his interest in the community and the future had returned.

Case 12. 514/53, age 54. Married farmer.

Hered. His father died of pneumonia at the age of 60. His mother was labile and emotional, her mood changing from day to day. A cousin of hers consulted the Psychiatric Policlinic of Uppsala concerning a neurosis she had. He was the only child.

Somat. Diseases. Always in good health. A moderate CO-intoxication in adult age without any resultant complications.

Somat. Findings in Aug., 1953: Undecided athletic type. Height 176 cm, weight 71 kg. Cor 0, blood pressure 135/90. Moreover, nothing noteworthy from a somatic point of view.

Psych. Intellectually normal. Vital and industrious. Manages a farm of 80 acres without any great difficulty. No asthenic traits. Not pedantic. Morning-active. Somewhat taciturn, but gets along well with people, and is warmly attached to his family. He is well adjusted to his position and feels at home in his neighbourhood. Of an even temperament. No special autumn and spring fatigue; during recent years, however, perhaps somewhat impatient and irritable.

Military Data. The patient completed his military training and extra compulsory service without remarks.

Case History. From a good home. No maladjustments as a child, nor during puberty. Born and brought up on the farm he took over after his father's death. Married in 1933. Matrimonial harmony. One son and one daughter of 14 and 19 years of age resp., who are sound and well-behaved. No abusus ethylicus. The first depression period occurred in the early spring of 1927 when he was 28 years old. His general condition was that of down-heartedness and anxiety, improving somewhat after a month. As an exogenesis there may possibly be adduced some trouble with his present wife. In 1952 a second period of depression set in, beginning in April and manifesting itself in fatigue, melancholy, and occasional weariness of life. Did not recover until October. No releasing factors this time.

Nor was there any external cause of his third period of depression—the one of main interest—which began in June 1953. The first indication of it was sleeplessness in the small hours, the patient awaking at about 3–4 a.m. without being able to fall asleep again, and then growing uneasy and brooding. His condition was worse in the mornings and better in the evenings. Suicidal intentions. On one occasion he tied a hangman's noose, but did not fulfil his intention. Symptoms of the mucous membranes. Dryness of mouth and eyes and incapacity for weeping. No noticeable loss of weight. No constipation. Loss of libido. On his being examined in August 1953, a moderate endogenous depression was discovered without too pronounced an inhibition. He claimed to suffer from an inferiority complex and, to some extent, self-reproach. After 3 el-shocks there was an obvious improvement. His uneasiness and anxiety vanished. His sleep returned, and the endogenous diurnal rhythm disappeared. Increased 1 kg in weight. Discharged on Aug. 30th in good health.

Post-examination on March 30th, 1954: The patient had fully recovered from his depression. Improved successively in the autumn. His courage and working-capacity now returned, as well as his libido. His sleep good. Seems to have a cheerful disposition, without any psychic rigidness.

Case 13. 644/53, age 42. Farmer.

Hered. His father was an alcoholist until the age of 40, when he became a Good Templar. He died in middle age from the Spanish Flue. His maternal grandfather committed suicide at an advanced age. His mother was nervous. 4/5 brothers and sisters.

Somat. Diseases. The patient suffered periodically from gastro-intestinal disturbances of a gastritis type every autumn and spring since he was a little more than 20 years old. A gastric ulcer was established for the first time in 1950. Op. Billroth II in May, 1953. No complications. Never bleedings. Otherwise, on the whole, somatically healthy.

Somat. Findings in Sept. 1953: Undecided type. Of good build. Height 179 cm,

weight 77 kg. Cor o. Blood-pressure 135/90. Scar on his abdomen from a gastric ulcer operation. Otherwise somatically and neurologically normal findings.

Psych. Intellectually normal. Industrious and energetic. He easily makes friends and gets on well with people. Is well-known for his easy-going manner. Gets things easily off his hands. Orderly without being pedantic. Perhaps somewhat hot-tempered. No asthenic traits, and of a somewhat emotional and lachrymose disposition. Interested and engaged in his community. Is a member of the Board of Child Welfare. No pronounced annual periods of depression, but he claims to be tired in the spring. Perhaps irritable in connection with gastro-intestinal disturbances recurring every year, particularly in the spring.

Military Data. The patient has completed his military training without remarks.

Case History. Growth and development normal. No maladjustments. Took over his paternal farm, which was rather small (15 acres of fields), but he got on well economically and liked his work. There was a certain irritation in relations with his brothers and sisters, as on several occasions he tried to buy their shares, but without success. He had an extra income as a caretaker of a school and as a churchwarden. Married at the age of 26; 2 sons, 10 and 15 years old, both healthy. Harmony in marriage. No sexual problems earlier. The patient's mild depressions in the spring assumed the character of a pronounced depression in the spring of 1953. Previously on two occasions (1947, 1949), in connection with his vernal anxiety, the patient had been suffering from psychosomatic discomforts of a sciatic type. In April 1953 there were pronounced difficulties in sleeping for the first time. He woke up in the small hours without being able to fall asleep again, brooding. At times his anxiety rose to the intensity of anguish. Could not get started in the mornings, and was hardly able to dress himself, having to be assisted by his wife. Uneasy, and feeling inferior, self-reproach, particularly concerning his farm, which he thought he ought to have got rid of earlier. His gastric ulcer took on a more serious character, and he was operated on, as mentioned above, in May 1953. The operation succeeded without complications and severe bleedings. Some improvement of his depression during the summer. No troubles whatever with his stomach after the operation. Grew worse during the latter part of the summer, causing his admission into the Clinic at the end of September. On exploration he revealed the picture of an endogenous depression. He had a prolonged time of reaction, was tense and obviously depressed. He harboured self-reproach and notions of inferiority. After 2 el-shocks there was an apparent improvement, though he was somewhat tense and insisted on going home to his work on the farm. He was discharged on Oct. 6, 1953.

Post-examination in March 1954: The patient did not prove to have recovered from his depression. Very soon after his discharge he had relapsed into his illness. His sleep was not satisfactory, and he had taken medicine uninterruptedly; he could hardly carry out his duties as a church warden, being reported ill. He did not consider himself able to manage his farm, but had put it out on lease. There was still now and then anguish before noon, even if he had certain bright days. When examined he was tense, possessing a mild but obvious psycho-motor inhibition. The syntonic trait of his personality was confirmed, and no psychic rigidness nor dullness of mind whatsoever could be observed. His libido has not returned.

Case 14. 648/53, age 48. House-painter. Married.

Hered. No definite heredity as to psychical maladies.

Somat. Diseases. On the whole healthy, apart from the Spanish flue, which was very mild.

Somat. Findings in Sept., 1953. Undecided habitus. Height 175 cm. Weight 68 kg. Cor o, Blood-pressure 130/95. EEG normal? His left leg is a few cm shorter than his right (Coxa plana). Ptosis bilaterally. Otherwise normal.

Psych. Premorbid personality. Intellectually normal. Always cheerful in his

work, easily makes contacts with people, but is of a somewhat reticent disposition. Particular, slightly pedantic. When healthy he is morning-active. Since the age of 40 he is a little tired in the spring.

Military Data. He has fulfilled his military service—being placed in group 4 on account of his hip—and also additional training.

Case History. Healthy as a child. No maladjustment, but walked in his sleep occasionally. Married in 1940. No children. Marital relationship good, however. No sexual problems. His first depressive period occurred in 1943 when he was doing extra military service. He grew uneasy and anxious, mostly in the mornings. Difficulties in sleeping of an endogenous type. Brooded and had an inferiority complex. Recovered after a month or two when he had finished his additional military service. The second depressive period turned up in the spring of 1947. His mother died on this occasion, and he was greatly affected by this loss. Grew more and more tired; his morning anxiety and uneasiness returned, and also an endogenous rhythm of sleep. Dry of mouth and constipated. On this occasion he had begun to build a new cottage for himself, worrying about it and regretting that he had ever started. He consulted a psychiatrist in the autumn of 1947 when his depression increased somewhat. He grew worse in the spring of 1948. Incapacity for work, feelings of inferiority and self-reproach. A moderate inhibition depression of an endogenous type was confirmed when he was admitted into the Psychiatric Clinic on March 30th, 1948. The depression diminished, and disappeared in the middle of June, the patient having then been treated with sedative insulin and opium. Was in good condition when discharged.—The third depressive period came in the summer of 1953, preceded by a moderate spring fatigue, this time without any releasing cause. He woke up early in the morning, having symptoms from the mucous membranes, a heavy head. His weight diminished a little. Imagined he had become overworked in 1948 from bulding his house. He thought everything was of no avail and felt sorry for his wife who had to put up with an invalid like him. He was admitted into the Clinic at the end of Sept., 1953. He was depressed, speaking in a low, anxious, monotonous voice, and manifesting a certain psycho-motor frustration. With regard to his endogenous picture, el-shock treatment was administered (6 shocks) showing good results. He felt more calm, and looked forward to his work with confidence. Was discharged in a good condition in the middle of October.

Post-examination in March, 1954: The patient was healthy and quite capable of working. Has had full-time work since his discharge. His sleep and appetite were satisfactory, but he had felt a little spring weariness during recent weeks, and a few mild disturbances returned in the forenoons. No anguish, nor pronounced frustration.

Case 15. 760/53, age 50. Foreman of a mill. Married.

Hered. His father died at the age of 54 from some kind of paralysis. Mother alive, 70 years old. A paternal cousin died at the age of 30 in a mental hospital. 2/4 brothers and sisters. A younger brother had a depressive period, which lasted for about a month and improved on medication.

Somat. Discases. On the whole healthy. Slight pains in his back in connection with the depressive periods, as below.

Somat. Findings. Nov. 1953: Undecided athletic type. Height 183 cm, weight 80 kg. Cor o. Blood-pressure 140/85. Neurology Lasèque 70° bilaterally. X-ray: Spondylosis deformans and disc degeneration in the back and lumbar region of the spinal column. EEG: Normal findings.

Psych. Premorbid personality. Intellectually normal. Somewhat melancholy. Ambitious and industrious, not pedantic. He is usually able to manage his job, is calm and confident, and attached to his family. Perhaps not so easy for him to make friends, but he is loyal. For several years, tired and pressed in his job in the autumn, possibly on account of a relatively great burden of work at that time.

Military data. Nothing noteworthy.

Case History. In childhood and adolescence nothing noteworthy. No maladjustment. Used hard drink a little too much before the age of 30. No abusus. In later years more abstinent. He is married and has a 16-year-old son. Matrimonial conditions: good conjugal relationship, warmly attached to his wife. No sexual problems. The first pronounced depressive period in 1949 occurred in connection with an increased burden of work. Became despondent, anxious, and uneasy. The period came in the late summer and autumn. He was able to continue his work after being free from it for a month, but had not fully recovered. During his gloomy periods he does not consider himself as vital as previously. A new depressive reaction with dorsal insufficiency occurred in the autumn of 1952 causing him to be confined to bed. The depressive period of chief interest began in August 1953, and the troubles were similar to those earlier, though more severe. Besides, for the first time, he had pronounced difficulties in sleeping. He would fall asleep at night, but woke up after midnight starting to brood with deep anxiety. Dryness of mouth and poor appetite. At the same time he grew more tired, nervous, and anxious. He felt his incapacity for working and asked to be exempted on account of illness. He suffered from an inferiority complex and reproached himself for not being able to be happy at home. He avoided people as he thought they could see that he was ill. When admitted to the Clinic he was depressive, and a psycho-motor frustration was confirmed. He had slight feelings of inferiority, a diurnal rhythm and uneasiness of an endogenous type in the small hours. Difficulties in concentration and a poor memory. He had good insight into his illness, did not seem emotionally cold, and had no symptoms of disintegration. He improved on treatment with histamine and sedative insulin, after which his depressive picture disappeared, but his psycho-somatic troubles became predominant. Numb feelings in his arms, and disturbances resembling sciatica, particularly in his left side on an obviously somatic anatomic basis, viz. a disc degeneration as stated above. Went home in January, but faced by the fact that he was discharged from his position, which he had held for 32 years, he broke down in a pronounced depression of a predominant inhibition type. His somatic troubles had now disappeared. Recovered after 5 el-shocks. Afterwards he said he had got rid of his depression, which had lasted during the whole autumn. Was sent home in good condition and spirits on Febr. 19, 1953.

Women

Case 1. 329/51, age 63. Wife of a chief lineman. 2 children.

Hered. Her mother, having an endogenous depression, committed suicide during a depressive state.

Somat. Diseases. Healthy, although having had pneumonia with a complication of post-pneumonic empyema about 1925. Usually not sensitive to infections.

Somat. Findings, June 1951: Dysplastic-pyknic type. Height 157 cm, weight 62 kg. Cor 0. Blood-pressure 140/90. X-ray of the lungs gave normal findings, and the vertebral column showed only an insignificant arthrosis deformans. Neurology: nothing noteworthy.

Psych. Intellectually normal. Her capacity for work when healthy was not below the level. Neither asthenic nor hysteric traits. Her personality is obviously syntonic. Since youth, periodically depressed almost every year in the autumn.

Case History. Childhood clouded on account of her mother's depressive condition. No neurolability nor maladjustment during her adolescence. — Fertile period at the age of 14–42. No gynecological disturbances and no severe climacterium. Not frigid. Her marriage is not quite happy, her husband being an alcoholist during certain periods. He suffered from a slight attack of diabetes some years ago, but

has always been able to manage his job. Good relationship with the two children, who are now socially well adopted. She is now a grandmother. — Her depressions since youth began gradually in Oct.–Nov. and she recovered successively during the spring. She feels tired, is despondent and frustrated, uneasy and anxious, and has inferiority complexes and suicidal intentions. Loss of appetite and weight, constipation, and restless sleep of an endogenous type. The periods as a whole are of a non-clinical type.

The depression of chief interest this time began in the spring, April 1951. — The clinical picture in June was that of an inhibition depression of the above-mentioned type, not very severe and manifestly on a decline. Endogenous diurnal rhythm (the pat. was usually morning-active), but her sleep was rather good on her arrival at the clinic. She was brooding "on everything and nothing", dry of mouth, thirsty. Recovered in a month after treatment with sedative insulin.

Post-examination in Dec. 1951: The pat. was rather healthy, but had had slight spring depressions again during the last few years. She is a little emotional, but well disposed, without any rigidness or dullness, and does not seem to be below the level.

Case 2. 601/51, age 59. Wife of a factory-owner, no children.

Hered. Mother as well as maternal aunt, nervous. A younger sister healthy.
Somat. Diseases. Healthy.

Somat. Findings. Sept. 1951: Dysplastic, undesignated type. Height 166 cm, weight 63 kg. Blood-pressure 120/100. Her hands and feet were remarkably warm in contrast to what is the case with exogenous depression and with asthenics. The usual findings concerning endogenous depressions. An X-ray established arthrosis deformans in the middle part of the column without reductions of the intervertebral discs. Somatology and neurology, nothing noteworthy besides that.

Psych. Intellectually normal. When healthy she was industrious and clever. Used to get on well with people. Extrovert with syntonic traits, and a disposition to have periodical states of depression.

Case History. No neurolability, such as biting her nails, nor enuresis nocturna, nor trouble with her sleep during adolescence. From a religious home. — Her mother forced her to join a Baptist denomination. No religious crisis, but she never felt at home in the congregation. Fertile period 14–48, coitus at 25. Her parents forced her into marriage, at the age of 31, with a man that she did not love. He too was religious. She was in love with another man, but remained faithful in her marriage, which was not quite happy. Childless, but she adopted a foster-daughter, who is now married and has children. — The pat. worked outside her home in the shop owned by the couple. She liked her job and managed it well. — The pat. was depressed in the spring since the age of 25. First attack of a more severe character at 40, accompanied by sleeplessness. After her menopause there was a long depressive period, 1938–39. — She was completely incapable of working, and was nursed in her home as well as at a convalescent home.

The period of chief interest began in the autumn of 1950, the pat. improving temporarily, but growing worse in connection with her mother-in-law's death during the New Year season of 1951. She felt remorse for not having shown her own mother enough love while she was in life. (Her mother died in 1933.) An influenza in the spring of 1951 made her worse. She was taken to the Clinic at the end of September that year, after being confined to her bed for the last few months. Strong delusions of sin and inferiority. Lost contact with God and was severely distressed by sin. Endogenous diurnal rhythm and difficulties in sleeping. "Worse before noon." Dry of mouth. "Cannot weep, but I want to." Constipation and poor appetite. After Suxil treatment, without any obvious results, ECT (3 shocks) was administered. Afterwards she recovered, and was discharged in the beginning of Nov.

Post-examination, Jan. 1954: Quite healthy and capable of working, but she has had a few slight depressions since she left the Clinic. Sleep and appetite satisfactory. Quite good contact with people.

Case 3. 657/51, age 33. Wife of building-worker, 2 children.

Hered. Mother religious, mentally depressed at times, particularly in middle age. Died of peritonitis after a cholecystitis operation. 2/3 brothers and sisters. Sister periodically depressed.

Somat. Diseases. Cholelithiasis, summer of 1947, 3 months' anamnesis. — Usually good appetite, can eat anything, never had jaundice. Urine never dark. — Subfebrile 1–2 weeks. Journal from Surgical Clinic: Diagnosis cholecystitis flegmonosa + cholelithiasis + pancreatitis ac. White corpuscle: 11,600. — SR 11 mm. Bilirubin 1.2 mg %. Slight pos. dir. reaction. Alkal. phosphatase 4 units. Tymol 0.7 units, Hanger ++. Slight pancreatitis, temporary. Op. cholecystectomia, no complications. — After operation, as earlier, no forms of discomfort in the hepatic region and no gastro-intestinal symptoms.

Somat. Findings, Oct. 1951: Dysplastic-pyknic type. Height 163 cm, weight 60 kg. Blood-pressure 140/95. Neurology: nothing noteworthy.

Psych. Premorbid personality. Intellectually normal. Morning-active, industrious, extrovert, usually gets things off her hands. Not self-confident, been fond of dancing and contacting people, but has possibly been somewhat emotional. No artistic interests, not hysterical. From the age of 20–25 generally depressed in autumn. Described as "obviously syntonic" at different psychiatric hospitals.

Case History. Broken home through mother's death when pat. was 14. — Sex debut at 16 with present husband. Partus I not yet 18, Partus II 1937, 2 healthy daughters. Sex life, no remark. Uses contraceptives. Not frigid. Healthy husband, 2 years older, whose sister was nursed in the summer of 1953 at a psychiatric clinic on account of a depressive psychosis and restored after ECT.

After mother's death, 1st period of depression at the age of 14–15, lasting about a month with anguish and poor sleep. In 1933, 2nd depressive period after first partus. In Sept. 1937, 3rd period of depression after 2nd partus. Was very tired, could not nurse, had anxiety, difficulties in sleeping, anguish during small hours, and suicidal intentions. — A 4th period of depression in 1944 came without any reason or exertion known. The same with her 5th depr. in 1946. She was treated on Febr. 13 to March 6 at Ulleråker Mental Hospital. Diagnosis: psychosis manico-depressiva. The clinical picture was a frustration depression. She had depressive misconceptions, self-reproach, delusions of sin, and vague suicidal intentions. X-ray: cor Tachycardi, confirmed as sinus tachycardi with certain S-T descents "sympaticotonus" on the ECG. — She had difficulties in sleeping and morning-anxiety. Was discharged as healthy after 3 electro-shocks. — In the autumn of 1947, the 6th depression. She was then treated in the Psychiatric Clinic. She came to the Surgical Clinic on Sept. 26 on account of a slight cholecystitis (see above), but she was so mentally depressed that the operation was postponed until she had recovered from her depression. After 3 el-shocks she was operated on without complications.

Her 7th period, of actual interest, occurred in 1951 when her eldest unmarried daughter was pregnant. — Now treated 3 times in the autumn at the Psych. Clinic for a severe frustration depression with self-reproach and a marked depressive trend of thoughts, but without suicidal intentions. There were symptoms in the mucous membranes, dryness of the mouth, incapacity for weeping, constipation. Hard to sleep, woke up at 3–4 a.m. in anguish. Obvious endogenous diurnal rhythm: "Mornings terrible." ECT, 4, 5, and 6 shocks resp., last ECT as block-shock. Sent home on 20 Dec. 1951. She was given policlinic ECT a couple of times in 1952, having not quite recovered. A slight depressive attack recurred in Sept. 1953.

Post-examination in Dec. 1953: Not quite healthy. Sleep and appetite mainly good. Complaints of vasolability. Sleep not good at times, and likewise her memory. Is mostly at home and can manage her household. No remarkable depression observed, but possibly a slight dullness and a certain psychic rigidness.

Case 4. 659/51, age 26. Wife of building-worker, 1 child.

Hered. Her mother nursed for an endogenous depression at the Clinic. Committed suicide at the age of 58, this being also the case with her maternal uncle and grandfather when they were of the same age. One sister epileptic. A twin sister had a slight depression at the age of 23. — No. 4/4 brothers and sisters.

Somat. Diseases. Always in good health.

Somat. Findings, Nov. 1951. Pyknic type. Height 157 cm, weight 70 kg. Blood-pressure 160/100, slight tachycardia: pulse rate 90–95. ECG and X-ray: normal findings. Furthermore, somat. and neurol. nil.

Psych. Intellectually normal. When healthy, she is industrious and clever. Felt at home and well liked by others in previous occupations. Agrees well with people, but has possibly been somewhat taciturn. No hysterical manifestations. She possesses syntonic traits, revealing an inclination for periods of downheartedness.

Case History. In good relationship with both her parents. From a religious home. No maladjustments. No religious attitude nor crisis. — Menarche at 14. Menses normal. Sex: not frigid, contraceptives. — Married at 22. One child, born in July 1951, healthy. Slight albuminuria and temporary high blood-pressure during the 5th month of pregnancy. Partus normalis. First depression of non-clinical type during her teens. "Not understood", incapacity for sleep, no loss of weight.

The next recurrence was in the autumn of 1951 two to three months after delivery. Arrived at the Clinic in Nov. having a pronounced inhibition depression with marked psychic and motoric frustration and total incapacity for work. Inferiority complexes: "No one as bad as I". Was brooding and depressed, had lost all hope of recovery, wanted to get away from everything, but could not leave her son out of pity. Lost her appetite, but felt thirsty, being dry of mouth. Could not weep. An obvious endogenous diurnal rhythm: "In the mornings it is so terribly dark". Lost her libido. Had a vague feeling that she was being talked about, but did not think she was thwarted in any way or persecuted. No schizophrenic symptoms. ECT 5 + 5 shocks of good effect. In the best of health when she returned home in Dec. A slight depression in the spring of 1952 accompanied by some despondency in the morning and inferiority notions of no clinical import.

Post-examination in Dec. 1953: Open-hearted and accessible. Not shy. Her will to live and her libido returned. Not "forgetful" as during her depression. Appetite and sleep, good.

Case 5. 710/51, age 55. Wife of farmer, 2 children.

Hered. Father somewhat nervous. 9/12 brothers and sisters, some of them having had transient nervous disturbances, and one sister with high blood-pressure.

Somat. Diseases. Healthy, except for rather severe diphtheria at the age of 14.

Somat. Findings, Sept. 1951: Dysplastic pyknic type. Cor 0. Blood-pressure 160/100 (below 150 on leaving hospital). It was ascertained that her hands were remarkably warm (in contrast to what is the case with exogenous depressions and in asthenics) — a discovery of great interest in differential diagnoses of endogenous depressions. Neurology: nothing noteworthy.

Psych. Intellectually normal, morning active, has always been industrious and a good worker. Managed the chores of a farm alone, besides her household. No hysterical traits. Syntonic with an inclination to getting moody in autumn and spring since the age of 40. Starts weeping easily.

Case History. No conflicts in her teens, nor in later years. Fertile period at the age of 14–52. No menopausic troubles. Two children and husband in good health. Attached to her home and family. Her husband has a sister treated for an endogenous depression, restored after ECT. — First period of depression in the spring of 1945 or 1946, 48 or 49 yrs. old, preceded by influenza. It was of an endogenous type with a diurnal rhythm. Difficulties in sleeping, especially during late hrs., the pat. being tired, frustrated and hypochrondric. Recovered somewhat in the afternoons. This period subsided after about a year.

Of good health until early in the spring of 1951, when a new depression set in, with certain gastro-intestinal disturbances of a cholic type in the beginning. X-ray: normal findings. Not having recovered after medicinal treatment during the summer, she was admitted to the Clinic in Sept. The depression was not too severe, being of a frustration type: "Am willing, but cannot". Dryness of mouth, esp. in the mornings. Complaints of rheumatoid pains in her arms and shoulders. Her sleep, having improved during the summer, was rather good, but she suffered from morning-anguish. — Was tired and without initiative, and could not drop the thought of being incurable on account of cancer. ECT, 5 shocks, yielded excellent results. The morning apathy of the patient and her rheumatoid aches disappeared. Increased 3 kg in weight, and her sleep was restful and refreshing. Sent home recovered in the middle of Oct. A preliminary post-examination in Nov. 1951 revealed good health without any despondency in the morning.

Post-examination in Dec. 1953: Subjectively in good health, cheerful, no dullness: "Now I remember things well". Weight increased to 67 kg. Good sleep. — The pat. claims to be industrious and healthy since her return home, but she had suffered occasionally from some despondency during the autumn and spring.

Case 6. 577/51, age 59. Wife of a carpenter, 3 children.

Hered. Father healthy, her mother had periodical abdominal trouble (no ulcus). Clever and industrious, but somewhat hot-tempered. No mental diseases in the family. 3/4 brothers and sisters, 2 having died young of the Spanish flu and inflammation of the kidneys.

Somat. Diseases. Physically healthy except for a catarrh of the stomach, which recurred regularly in autumn and spring since the age of 20. (On a routine X-ray examination in 1945 there was accidentally revealed a calcified t.b.-focus with a slight fibrosis on the apex of the right lung.)

Somat. Findings. Sept. 1951: Undesignated type. Height 163 cm, weight 56.5 kg. Blood-pressure 125/75. Somatology and neurology: normal findings.

Psych. Intellectually normal. Clever and industrious. Was able to manage her home. Sociable. Lively in the morning. When younger she was somewhat hot-tempered and easily offended. Not anxious, tense, nor unconfident in herself. No interests in art or intellectual matters. Usually not considered hysterical. Periodical abdominal discomfort as above. Syntonic traits with a tendency towards periodical depressions.

Case History. No maladjustments as a child. Confirmed at 14. No religious interests or crises. Sexually, nothing to note. Menses regular. Menopause in 1940 at the age of 48. Married at 19. Harmony and good sexual relationship in marriage. Husband healthy, kind, and considerate. One son born in 1912, imbecile. Twin-birth; the other twin died. Two healthy sons born in 1930 (twins). One miscarriage in 1920. No external conflicts except that she worries about her imbecile son, who is sometimes irritable and tiresome. First pronounced period of depression at the age of 48. Grew tired, exhausted, "couldn't do anything", nor "get to it" in a cheerful spirit as previously. After that, she had typical periods of depression in May–June every year, improving during autumn and winter. Between these periods she was able to work and be active. On account of an endogenous

depression she was treated at a psychiatric clinic in the autumn of 1950. She revealed an endogenous diurnal rhythm. Difficulties in sleeping: woke up at 3–4 a.m. with anxiety. Hard to get started before noon; better in the afternoon. Particular symptoms: Dryness of eyes and mouth. "No tears." Wanted to weep when she was sad, but could not. Constipation, loss of weight, always thirsty. When examined she was frustrated and obviously depressed. Worried about her imbecile son as well as her other two sons on account of their military conscription.— Discharged as healthy after ECT, 3 shocks. Was treated for a second period of depression in the autumn of 1951, the period of chief interest. The pat. was sound after being discharged in 1950, but her usual spring depression set in again in May. As she grew worse during the autumn, she was admitted to the Clinic for an ECT on Sept. 19–Oct. 17. The clinical picture was that of a slight frustration depression with diurnal rhythm but without any pronounced symptoms of the mucous membranes. She was also somewhat lachrymose. She brooded on suicide in the mornings. Improvement after 6 shocks, yet without any obvious increase of weight.— Was admitted for her first post-examination at the end of Nov., being then not quite recovered, according to her husband. Unenterprising and somewhat frustrated, with an obvious diurnal rhythm. After another 3 el-shocks there was a remarkable improvement. In good condition on being discharged on Dec. 13, 1951.

Post-examination, Jan. 1954: The pat. was capable of working and in rather good condition (1952). Another depression in 1953 grew worse during the autumn, causing her to be taken to another mental hospital late in the autumn. In the journal it is recorded that the clinical picture was the ordinary one. ECT was started with a positive result. No schizophrenic symptoms were to be seen in the picture.

Case 7. 396/51, age 40. Wife of farmer, one child.

Hered. Nothing noteworthy. Her parents are psychically sound. She is the only child.

Somat. Diseases. Healthy, apart from childhood-diseases.

Somat. Findings in July, 1951: Pyknic type. Height 165 cm, weight 58 kg. Cor 0. Blood-pressure 170/110—at a later test 150/100. Otherwise nothing noteworthy from a somat. and neurological standpoint.

Psych. Premorbid personality. Intellectually normal. When healthy, industrious and efficient, and gets on well with people. Syntonic with slightly hysterical traits. Feels at home in her family. Not asthenic, not pedantic. Perhaps always somewhat lachrymose and emotional.

Case History. Good conditions in her childhood home. No maladjustments nor crises in adolescence. Menarche at 14. Menses regular except on one or two occasions during her depressive periods. Married at the age of 20. Marriage happy, not frigid. One daughter 13 years old, delivered by forceps. Her daughter is somewhat labile, but otherwise healthy, as is her husband. Her economy was good. The couple manage a farm of 33 acres together with the patient's parents. The first depressive period occurred in April 1951. On this occasion the patient had been told that she had a slight myoma and became excited on account of this. Her condition was partly of a psycho-somatic character in the form of gastro-intestinal discomforts. Further, she grew despondent and frustrated with an obvious endogenous diurnal rhythm. She lost her sleep at night: woke up at about 4 a.m. with a feeling of anguish, lost her appetite, lost weight. She harboured the delusion that she was afflicted with cancer; and she also had hypochondriac ideas. On her admission into the Psychiatric Clinic in July 1951, a syntonic constitution was observed, as well as a depressive picture with a moderate inhibition, and at the same time a temporary and rather pronounced tension. An acute anxiety motivated ECT (5 shocks and 2 absences). The inhibition disappeared, but she was still a little tense, and an apparent lability after the shock-treatment was to

be noticed. No negativism. "She cheers up the whole ward with her gentle nature." Was discharged at the end of July, but not quite recovered, her poor sleep and endogenous diurnal rhythm still remaining. Was admitted again in August, and was given another few shocks, sedative insulin treatment, and a subsequent cure with suxil. Was discharged in rather good condition on Sept. 11, after which her condition was somewhat fluctuating with a depressive reaction during the following half-year; but she was healthy, vital, and morning active during the greater part of 1952, and until late in the autumn of 1953. The last depression was possibly released by anxiety for her now 17-year-old daughter, who had been afflicted with a period of sleeplessness after exacting duties.

Post-examination in Jan., 1954: The patient was not quite healthy and well-balanced. There was no deep depression, but she had a certain depressive dysphoric reaction. Her endogenous diurnal rhythm returned as well as difficulties in sleeping, and she said it was difficult to manage her home. A new series of shocks was taken into consideration in case her condition grew worse during the spring.

Case 8. 196/52, age 60. Wife of a mason, 3 children.

Hered. Father healthy, died in old age, mother died, 52 years old, of pneumonia after the Spanish flu. 1/6 brothers and sisters. No mental diseases known in the family.

Somat. Diseases. On the whole healthy.

Somat. Findings. March 1952: Pyknic type. Stout. Height 161.5 cm, weight 82.5 kg. Cor 0. Blood-pressure 165/120. ECG as well as X-ray control normal. Somat. and neurol. findings: nothing noteworthy except for a spondylosis deformans of the columna vertebr.

Psych. Intellectually normal. Morning active and vital. No asthenic traits, not particularly labile nor emotional. Gets on well with people, and participates with great interest in sewing-circles, etc. Cheerful and accessible. Makes friends easily. Obvious syntonic traits with a tendency towards slight dejections in spring and particularly in autumn, during maturity.

Case History. No maladjustment as a child, nor during her teens. No religious outlook nor crises. Menarche at 14, menopause at 49. No trouble with her menstruation. Married at 22, 3 children, 1 son and 2 daughters, healthy. Harmony in marriage. Not frigid during her fertile period. Husband healthy. No external conflicts. The patient's above depressive periods became more pronounced at the age of 55, 5–6 years after her menopause—with anguish, anxiety, and hypochondriacal ideas, particularly during autumns. Used to wake up at 5 to 6 a.m.—earlier than normal—brooding. "Always well and calm in the afternoon."

The depression of chief interest occurred in Oct–Nov., 1951. Periodically a panic-stricken anguish intermingled with a dull sense of dread and uneasiness. Poor appetite. Symptoms of the mucous membranes: dry of mouth and thirsty, but was able to weep. Lost weight. Was afflicted with an inflammation of the upper air-passages at Christmas time. Further degeneration in Jan., 1952, when she came to the Clinic and was nursed during Jan. 8 to Febr. 13 on account of an endogenous depression. At the same time she had a septic bursitis praepatellaris. Was febrile for about 24 hours. Was given a penicillin treatment. A slightly raised SR (max. 36 mm/1 hour); subsided successively.—The pat. was discharged, after improving somewhat without ECT, but grew worse in Febr.–March, and was therefore readmitted to the Clinic on March 14. The clinical picture was of a depressive character with traits of tension and agitation. Diurnal rhythm as earlier, but the inhibition before noon was partly overshadowed by the patient's anxiety. Sleep somewhat satisfactory. Her weight was 3 kg less than when first taken to the Clinic. After 5 el-shocks she was in rather good condition. "No anguish any longer." Cheerful and felt healthy. Was discharged on April 9.

Post-examination, Febr. 1954: In good condition and, as certified by herself and

her family, quite recovered; able to work and cheerful, as prior to her illness. The pat. claimed she did not feel her health had quite returned until the summer, but since then she had been "as well as ever before". Appetite and sleep satisfactory. Weight constant. A test by the doctor at her domicile revealed a blood-pressure of 150. The pat. is spontaneous, communicative, accessible, and does not seem to be below the level. Emotionally pliable and well-disposed.

Case 9. 206/52, age 39. Wife of caretaker. One child.

Hered. Her father was an alcoholist, having several times been treated at an institution for inebriates. Her mother was nervous. 2/5 brothers and sisters, who are healthy and well adapted.

Somat. Diseases. Scarlet fever at 12 years of age, no complications. Otherwise healthy.

Somat. Findings in March, 1952: Of a pyknic type. Height 159 cm, weight 60 kg. Cor 0, blood-pressure 145/80. Somat. and neurologically normal conditions.

Psych. Premorbid personality. Intellectually normal. Likes working, cheerful, and is fond of singing during her duties. Emotional type, occasionally not finding it easy to dispell her problems. Not bashful, nor reserved. Tidy, but not pedantic. Predominantly syntonic constitution with a tendency to becoming depressed in the spring.

Case History. Parental home not happy owing to her father's alcoholism. In spite of this, there was no maladjustment in her childhood. No crises during puberty. Married at 25. Her husband healthy as is her son. Good relationship in marriage, not frigid. Menstruation regular, no gynecological disturbances, but used to be somewhat irritable before menses. Her economy good, no external conflicts.

Her first depression period occurred in 1940 after the birth of her child (no haemorrhage, no complications). Became tired, could not sleep, and lost weight. Could not take care of her child. Self-reproaches for being a bad mother. Her depression was over in a few months. Since then she generally suffered from mild ones during a few weeks in spring. Her second depression period came in 1949, being possibly released by her sister-in-law's suicide and in connection with her taking care of the latter's son, who was a little troublesome. Grew tired, found it difficult to sleep, and did not get well until after half a year.—In 1950 there was a third period of depression. After being tired for some time, numb and pricking sensations as well as a little giddiness turned up in the beginning of April of the same year. Simultaneously she had some compulsive neurotic traits, being afraid of doing herself and her relatives harm. These traits often occurred at the beginning of her more pronounced depressions. Felt at the same time parched in her throat, revealing an endogenous diurnal rhythm, and suffered from severe morning anguish. Was admitted to the Clinic in May, manifesting an inhibition depression and somewhat compulsive neurotic traits. A syntonic constitution was found. After ECT (4 shocks) she was discharged, yet not quite recovered, and was examined policlinically. Periodically still uneasy, brooding in the belief that she was insane. Thought she was not understood by her husband, and had sexual problems. A few days' observation at the Clinic in August confirmed the fact that the depression had practically subsided. A mild depression in the spring of 1951 was completely cured after el-shock.

The fifth depressive period—the one of chief interest—appeared in the spring of 1952. The same picture as before with depressive thoughts, and psycho-motor inhibition to a moderate degree. Her feelings of inferiority were pronounced, but she had no delusions of sin. Longed to die for altruistic reasons, wanting to relieve her husband of "his worthless wife". After being treated with histamine for a period of about 12 days, during which her depression was mitigated, she

was given ECT (2 shocks). A stabilization of her general condition made it possible for her to take part in her husband's 50th anniversary festival. Post-treatment with histamine resulted in good health. Increased a few kg in weight, and was discharged in good health in May.

Post-examination in Dec., 1953. After being sent home, the patient claims to possess good health. No noticeable spring depression this year. Cheerful, optimistic, being able to manage her home without any difficulty. Pregnant again, expecting her second child in April 1954. In spite of her previous depressions the child is longed for. Healthy during these first four months of her pregnancy.

Case 10. 9/52, age 62. Widow of store-room manager, one child.

Hered. Parents died at about 70, psychically sound. 5/9 brothers and sisters, 2 died as infants, 2 from somatic diseases, 4 living, healthy. One brother schizophrenic since youth, at present being treated at an old people's home.

Somat. Diseases. Always in good health, except for suffering from a rheumatic affection at about the age of 20 accompanied by an increase of the SR. She claims never to have been treated at a hospital for this. A slight cardial hypertrophy ascertained in 1942 roentgenologically. However, this was not confirmed in 1952, thus establishing normal findings. During her depressive states she had a temporary hypertonia when agitated.

Somat. Findings, Jan. 1952: A pyknic, dysplastic type. Height 153 cm, weight 54 kg. A certain systolic cardial murmur with its maximum on the apex. Blood-pressure about 210/110 on her arrival at the Clinic, and 180/90 when dismissed.

Psych. Intellectually endowed, extrovert, cheerful and sociable. Mixes in society when healthy. Not hysterical. Syntonic traits with a pronounced tendency to periodicity since the age of 40.

Case History. Parents' home good. No maladjustment during adolescence. Fertile period: 14–50. Not frigid. Menses always normal, no gynecological troubles. Married at 23. Harmony in marriage. One son healthy, socially well adapted. Personal afflictions: her husband's illness and death of tumor cerebri, 1938, operated on in 1937. — Prior to her husband's illness her periodicity was more pronounced with periods of depression and slight hypermania. In 1941 an attempt at suicide by gas. Treated in 1942–52 each, or every other, year for one or two months, respectively, at Ulleråker Mental Hospital or at the Psychiatric Clinic, the diagnosis being psychosis manico-depressiva. ECT always of a good effect. Was administered about 30 schocks in all during the course of 8–9 periods. Each time she completely recovered. These period generally began in spring and autumn, setting in gradually with weariness, anxiety, suicidal brooding, and later developing into predominant massive frustration. Endogenous diurnal rhythm, symptoms from the mucous membrane, accompanied by loss of appetite and one or two kg of weight. Woke up in anguish during the small hours. On a few occasions raptus melancholicus and attempts at suicide.

The depression of main interest set in during Nov. 1951, and was of the usual type she had. She suffered from inhibition, and was given two shocks policlinically in Dec. But not getting better, she was admitted into the ward. Her diurnal rhythm had been mitigated and she could sleep rather well in spite of a rather severe inhibition depression. After being treated with histamine, 1 1/2 mg four times a day during a fortnight, she was cured by ECT, 3 shocks. Obvious turn for the better after 2nd shock. — New depression in late spring and summer requiring ECT again at hospital. Complete recovery.

Post-examination in Dec. 1953 revealed good health. Remarkably well preserved, gentle and well disposed. Memory good, and she seems to be on a normal level. Working-capacity good.

Case 11. 31/52, age 42. Wife of merchant, 2 children.

Hered. Mother somewhat nervous, especially during her climacterium. Father healthy. Three brothers and sisters, quite well and socially adapted.

Somat. Diseases. Of good health, but suffered from sinusitis a couple of times without any conscious disturbances afterwards.

Somat. Findings, Jan. 1952: Undesignated type. Height 164 cm, weight 60 kg. Blood-pressure 130/95. Neurology: nothing noteworthy.

Psych. Intellect normal. Morning-active, is able to attend to her family and is sociable. No asthenic traits, nor hysteric. Often a little irritated during menses, having head-aches. Not pedantic. Extrovert. Predominantly syntonic, inclined to being moody in autumn and spring.

Case History. Parents' home good. No maladjustment. No religious crisis, nor trouble in her teens, except for slight restlessness in her sleep. No nightmares. Menarche at 15. Menses regular. Married at 24. One son and one daughter, healthy, born in 1942 and 1947 respectively. Not frigid. Harmony in her marriage except during her depressive states when thinking she was not understood. Her repeated seasonal depressions were initially of a non-clinical type. The first depression requiring treatment occurred after her first partus in Dec. 1942. In the winter and early spring of 1943 she was melancholy, tired, anxious, and had no good sleep. Cured by ECT, recovering in the autumn. The 2nd depression came on in 1947 after her second partus (each time partus normalis). On this occasion, not so severe.

Her 3rd depression occurred in the spring of 1950 in connection with much work and illness in her home. She also suffered from a slight infection during this spring. Grew tired, melancholic, having no strength to do anything. She was given six el-shocks at a mental hospital without recovering. Endogenous diurnal rhythm and difficulties in getting started in the mornings. Was slightly irritable. Could not sleep well. Suffered from headaches and was treated by various doctors without regaining her health. Depressive trend of thoughts and inferiority complexes. — At the clinical examination in Jan. 1952 the following was revealed: depression of an endogenous type. Moreover, the pat. was somewhat labile, indicating an anaesthesia dolorosa: had no feeling for her husband, and especially not for her children, on account of which she grieved. She had lost her libido. Complained of a dry mouth and thirst. Despondent and brooding. Treated with ECT, 7 + 6 shocks with good results. Increased in weight about 3 kg and was discharged in March.

Post-examination in Jan. 1954: The pat. declared she had been quite well since returning home. She and her husband said that it was long since she had felt so well. Regained her will to live. Managed her house easily and enjoyed social activity. Her morning spirits returned, and she slept as a rule well. She is obviously syntonic and on a normal level, complaining however of a slight lack of memory.

Case 12. 153/52, age 28. Wife of building-worker, 2 children.

Hered. Father somewhat stern and hot-headed. Mother had a depression at about the age of 40, lasting for a year. Had also cholelithiasis, and used to be tired in the spring. 4/5 brothers and sisters, socially well adapted, and healthy. One sister was a little nervous.

Somat. Diseases. Maxillary sinusitis in 1949, not so severe. Apart from this she was of good health. Never anaemic, nor sensitive to infections.

Somat. Findings, Febr. 1952: Pyknic type. Height 163 cm, weight 67 kg. Rather obese. Cor: 0. Blood-pressure 140/90. EEG: (control in Dec. 1951). Occipital alpha frequency could not be counted because of poor representation. No focus nor asymmetry. Occasionally it was relatively abundant with low rapid activity.

Parietally some relatively low episodes of about an activity of 10/sec. with upwards topped and downwards pointed waves reminiscent of Gibb's hypothalamic activity. Temporarily quite a good deal of rather low irregular activity of 2–5/sec. Hyperventilation: 0, but stroboscopy yielded a relatively frequent representation of low high-frequency activity. Pathological findings?

Psych. Intellectually on a normal level. Morning-active when healthy. Industrious but somewhat emotional. Attached to her husband and children. Cheerful, accessible, and light-hearted, but used to be somewhat irritable before and during her menstruation. Syntonic traits with a tendency to being a little melancholic in the autumn.

Case History. Parents' home good, but some disturbances on account of her father's temper. No maladjustment during her adolescence. No religious broodings. Menarche at 13, nothing noteworthy. Menses regular, but the pat. is generally irritable, tired, and a little moody, feeling somewhat queer, as mentioned above. Not frigid, contraceptives. First coitus at 19, married to the same man at 20. Two children: son and daughter, born 1944 and 1951 respectively, healthy. Her boy was somewhat unruly. — Some transient unadaptability in the beginning of her marriage. Her first nonclinical slight depression occurred in her teens, lasting for about a month. Did not think she was understood. Avoided people, having at the same time difficulty in sleeping. No nightmares. After the 2nd partus in March 1951, she became depressed, finding it difficult to sleep. — A certain improvement during the summer, but degeneration again in the autumn. She grew tired and could not manage her household, was melancholy, thought she had no right to live, being "a burden to all and in their way". Simultaneously she was afflicted with certain anguish. Her condition fluctuated, but the mornings were always the worst: "Somewhat calmer in the afternoon, feeling more easy." Her restlessness during menstruation persisted and was more pronounced. Symptoms in the mucous membrane, dryness of mouth and throat, difficulties in falling asleep as well as those of sleeping in the small hours. — At the clinical examination at the end of Febr. 1952, psychomotor frustration was ascertained. She was depressed, having inferiority complexes, and confessed that she had been brooding on taking her life with gas. — ECT, 5 shocks. Her depressive picture disappeared; her activity in the morning also returned, and she regained her capacity for joking. But she was irritable and her memory was poor (cf. EEG-findings). Sent home after post-treatment with histamine and Suxil, being in a relatively good condition. Completely recovered during the summer. Turned hypomanic in the summer of 1953. Refused to live with her husband and left home. Hyperactive, quarrelsome, with an increase of her libido. After some time she took some work at another place. Was checked and treated in the policlinic as well as with the assistance of her relatives. Returned to her family after two or three months when her period was over.

Post-examination in Dec. 1953 showed good health. Now has mental balance, is well adapted and sociable. Her syntonic trait was confirmed. Her weight was constant, sleep and appetite good.

Case 13. 316/52, age 31. Wife of an ordnance-officer. One child.

Hered. Father alcoholist, mother living, age 74, healthy. 9/9 brothers and sisters. One sister had a depression in connection with matrimonial conflicts, age 32.

Somat. Diseases. Always healthy except for a complication after partus 1944: Placenta persistens, which caused bleedings. Restored after curettage.

Somat. Findings, May 1952, undesignated type. Height 161 cm, weight 53 kg. Blood-pressure 145/95. Neurology: nothing noteworthy.

Psych. Premorbid personality. Intelligence normal. Not "asthenic", nor nervous. Calm and usually of an even temper. Accessible. Neat without being pedantic. Sociable and easy to get on well with. — Not particularly suggestible, nor hysteric. — Usually tired in spring. Syntonic traits.

Case History. No maladjustment in childhood, nor during adolescence, although family life was disturbed by father's alcoholic habits. Not a religious home, no personal attitude to religion. — Menarche at 14, menses regular and normal except for first year. Coitus at 20, married at 21. Good connection with husband. Not frigid. No economic troubles. First period of depression at 21 with anxiety and headaches. Had much to do as an assistant shop-keeper and as a house-wife. Husband at this time still studying. Since 1943, sometimes spring depressions with anxiety in the evenings as she was going to sleep. But mornings worst. Brooding, no sleep in the small hours and could not get started in the mornings — not the case normally. Better in the afternoon. Pressure on the chest and certain dizziness before noon, "everything piled up then". — Symptoms from the mucous membranes, thirst, and constipation. Appetite poor. Came first to a psychiatrist in the spring of 1950; next time in 1951, being treated in the Clinic during 3 May–5 June, 1952.

A slight psycho-motor frustration was noticed. She was very tired, had depressive thoughts, was afraid of becoming insane. Not self-confident and somewhat dull of mind. No disintegration and no obsessive symptoms, nor any Beziehung. At times her tension was predominant, and she complained of dryness of the mouth and palpitations of the heart. Pulse-rate: max 90/min. — Difficulties in sleeping, and an endogenous diurnal rhythm. She was first given histamine treatment, 1 1/2 mg 4 times daily for 14 days, and a considerable improvement in her depressive reactions was noted. Afterwards, 16 days' sedative insulin treatment (max. 48 units) in order to mitigate remaining tension, also with good effect. Returned home in rather good health.

Post-examination, Jan. 1954, 1 1/2 years later. Pat. is subjectively quite healthy. She remembers the details of her depression very well, claiming she had the idea she was incurable. Not had any depression since 1952, but the one occurring that year was not quite over until late in the summer. Pat. is emotionally tender, and no psychic rigidity is noticeable. Syntonic.

Case 14. 326/53, age 55. Wife of agricultural worker, 5 children.

Hered. 1/5 brothers and sisters, 2 living.

Somat. Diseases. Sound and healthy, but since the age of 19 nervous and restless in autumn and spring. Suffered particularly from abdominal troubles, such as rumbling and distention. X-ray examination in 1931 revealed ulcus duodeni. In Jan. 1948 operated on: Bilroth II without complications, never melaena. Nervous and restless after op. in spring. — Sept. 1952, cholecystitis ac. + cholelithiasis: op. cholecystectomia, 3—4 day's anamnesis. Non-icteric; laboratory findings: Bilirubin 0.9 units, Direct reaction neg. — Alk. phosphatase 12 units. Afterwards no abdominal discomfort.

Somat. Findings. May 1953: Pyknic type. Height 160 cm, weight 77 kg. Cor 0. Blood-pressure 170/90. Somatically nothing noteworthy. Reactions of the liver in blood and urine, normal findings.

Psych. Intellect good. Her work efficient, she does not feel flurried. No feeling of insecurity, cheerful, and of an even temperament. Not hysterical. Syntonic and periodically despondent.

Case History. Parents' home good. No maladjustment. Menarche at 14. Menses normal. Married at 25. Five children born in 1923–1932, healthy as well as her husband. — Economy good, but pressed by a great burden of work. Good connection in marriage. Not frigid. Not yet entered menopause. — After the above operation for ulcus the patient's nervous troubles took on a depressive character. Found it hard to sleep and was uneasy in the spring of 1948. Treated for a depression of a mixed type. Removed to the Clinic after an attempt at suicide early one morning in August. Morning anguish, poor sleep in the small hours. Certain difficulties in falling asleep. Tired and without initiative. Angor

and certain temporary agitation and motor anxiety. Could not weep, although she wanted to. After ECT, 3 shocks, quite restored from her depression. Op. cholecystectomi within a month after her discharge from the Psychiatric Clinic.

Healthy till Febr. 1953. Tired as previously, was able to sleep, but woke up in the small hours and lay as in a state of drowsiness; anguish in the early morning and before noon. No tears: "If I could at least weep!" Menses irregular during her depression. Loss of libido, as during the first period. When taken to the Clinic on August 7th she had a moderate depression of a mixed type, as above. Bad sleep, but above all subjectively tired and incapable of working. After a histamine treatment she was discharged as quite well on May 7th.

Post-examination in Jan. 1954: Sound and healthy, "everything runs so smoothly". Libido returned. No gastro-intestinal disturbances, but the pat. avoids fatty food. Sleep and appetite good. Now no gloomy thoughts any longer.

Case 15. 355/53, age 30. Wife of engine-driver, 4 children.

Hered. Mother periodically depressed, espec. in the autumn. Father had asthma bronchiale. One brother committed suicide at about the age of 30. 5/5 brothers and sisters.

Somat. Diseases. In general healthy.

Somat. Findings, May 1953: Pyknic, undesignated type. Height 158 cm, weight 86 kg. Female obesity, firm in flesh. Neurology: nothing noteworthy. Hypochylia gastrica on arrival at the Clinic. EEG: normal findings? Tendency towards an alpha of high frequency, and solitary interspersions of an activity resembling spikes having about half their height. O effect on hyperventilation.

Psych. Premorbid personality. Intelligence a little below the level. Industrious and efficient. Cheerfully extrovert, enjoys company, and has no difficulty in adapting herself to conditions. Well liked. Occasionally somewhat emotional in her temper. Syntonic traits, the pat. having a tendency to being a little gloomy in autumn and spring.

Case History. Neurolability as a child with enuresis nocturna until the age of 8–10. Her sleep at night a little uneasy during her early teens and in the spring. Menarche at 14. Menses regular, as a rule, but can vary about a week during her depressive states. No gynecolog. disturbances apart from these. Married at 19. Husband healthy as well as her children, born 1942–51. The latest child not wanted by the pat., owing to her repeated depressions. The pat. claims to have a slight tendency of being a little over-active "when healthy". Some trouble during the first period of her marriage. Her husband unfaithful immediately after the birth of her first child. By mere accident, this was later also the case with the patient on a single occasion one spring when depressed and somewhat desperate. During her autumn and spring depressions of recent years she reproaches herself severely on account of this. Otherwise she enjoys a good marriage-relationship.

The depression of chief interest began in Febr. 1952. She grew despondent, melancholy, and tired, brooding upon her brother's suicide, and thinking she had been the cause of her brother's death by her unchaste life, as well as remembering what her sister-in-law, the widow of her brother, had told her at the funeral. Felt better, but not quite well in the summer. During early spring (1953) fluctuating conditions of depression, accompanied by anxiety and occasionally agitation and aggressiveness. In May, degeneration with a predominating inhibition: incapable of working, no longer had any feeling for her husband and children. Loss of libido, endogenous diurnal rhythm, incapacity for sleeping during the small hours, and anxiety before noon. On examination at the clinic in the middle of May, her condition was that of a rather severe inhibition depression with psycho-motor frustration. Difficulty in concentrating, but no disintegration nor obsessive symptoms. She was intially treated with histamine, 1 1/4 mg four

times daily for 14 days, but having not recovered from her depression, she was given ECT with good results. "I feel the shocks have put everything straight again." No endogenous diurnal rhythm any more. Sent home in good health.

Post-examination, Jan. 1954: Healthy, sleeps well. Weight constant. Sociable and of a cheerful disposition. Obviously syntonic. Got back her will to live as well as her libido. Happy with her husband. Can manage her household easily alone, doing also extra work outside her home.

Case 16. 358/53, age 25. Wife of farmer, 3 children.

Hered. A paternal aunt committed suicide after a lengthy period of depression, another patern. aunt epileptic. One patern. uncle periodically depressed and incapable of work. 2/8 brothers and sisters healthy.

Somat. Diseases. Nothing noteworthy (dermatofibroma antecrur sin., op.: Excis. 1951).

Somatic Findings, May 1953. Dysplastic — undecided type. Height 176 cm, weight 71 kg. Cor: normal findings. Blood-pressure 135/100. EEG: Occipital alpha-frequency 11/sec., a rather poorly organized curve with periods of slow alpha (8/sec.).

Psych. Intellectually endowed. Of a cheerful disposition, accessible, industrious and healthy. Gets along well with people. A little pedantic, at times somewhat irritable premenstrually (cf. EEG findings and heredity). No asthenic symptoms in spite of very hard work, except possibly during her spring depressions since 1941. Usually gets up early in the mornings.

Case History. Childhood home unhappy. Father hot-headed and aggressive. No maladjustment during adolescence, but she suffered from disturbances in sleep and from nightmares periodically during her teens. Menarche at 13. Menses normal. Three healthy children. First child at 18, the year of her marriage. Husband healthy. Good connection in marriage. Not frigid, contraceptives.

First Depression in April 1949, one month after 3rd partus. Grew tired, depressed, restless in sleep, and suffered angor. Subsequently a spring depression requiring treatment at the Clinic, 1951. ECT was administered yielding good results. The pat. was initially "blurred" (EEG dysrhythmia!), but she herself claims that she could now sleep for the first time for many a day, after receiving the shocks, and that she felt happy.

The actual depression of 1953 started in Febr.–March. The pat. felt anxious, could not set herself to doing anything in earnest. Woke up early in the morning brooding, "afternoons better", but she also found it somewhat difficult to fall asleep. Predominant frustration. She suffered from depressive delusions, harbouring suicidal intentions. At the Clinic in May 1953 she considered herself to be inferior in many ways, worrying over the fact that she was not a good mother and reproaching herself for not having nursed her babies sufficiently. Felt excluded and not understood. No symptoms of disintegration. No obsessive symptoms. — As an exogenesis it may be adduced that she had a great load of work and that unsatisfactory conditions in her home tormented her: Living quarters were shared with her parents-in-law, and she was not accepted by her mother-in-law, especially in the beginning of her marriage. — After psychotherapy and treatment with insulin, opium, and hormones she was discharged from the clinic in good health in July.

Post-examination in Dec. Quite healthy. Well-dressed, tidy, accessible and cheerful. Regained her bright outlook on life and her confidence. The syntonic traits of her personality were confirmed.

Case 17. 387/53, age 39. Wife of a saw-mill worker, 2 children.

Hered. Mother mentally depressed in spring and autumn. Father alcoholic. 2/3 brothers and sisters, in good health.

Somat. Diseases. Usually healthy. Slight rheumatic reaction, 1946, after angina tons. At home some weeks, SR max 10 mm/1 hour. No trouble with her joints. Afterwards no rheumatic symptoms.

Somat. Findings. Febr. 1953: Pyknic type. Height 169 cm, weight 60 kg. Cor: psychically and roentgenologically normal findings. ECG: slight sinus tachycardia with minute S-T descents, "sympathicotonia". ECG eliminates coronary disease. — Blood-pressure 180/100 and, later, below 160/100. A neurological examination yielded normal findings as well as an inspection of her eyegrounds. — In her urine there was no urobilin nor urobilinogen. EEG: occipital alpha frequency 9/sec. Normal findings.

Psych. Premorbid personality. Intelligence good. Usually cheerful and bright, in the mornings, too. Industrious and efficient. Practical. Also been weaving and sewing for others. Gets on well with people. Likes music, but does not play. Periodically somewhat emotional and weeps easily at times. — Not hysterical. — Since the age of 35, light depression in autumn. Tired and moody. "Housewife complex" and inferiority complex. Felt "washed-out". Cannot get started in the mornings (autumn). In summer she can "tackle anything" without exertion.

Case History. Parents' home not good because of her father's alcoholism. Enuresis nocturna until the age of 6. Menarche at 16 (like her mother). Menses normal. Married 1938. First child the year before with present husband, 2nd child 1939, both healthy. Marriage happy. Sex: not frigid, contraceptives. No economic problems, but had much work for some years when she took care of her senile father, who died in 1950.

The depression chiefly to be examined started in Oct. 1952 with weariness and anxiety, especially in the mornings. At the same time lack of initiative and had difficulties in sleeping. Woke up at about 3–4 a.m. in anguish. Was also very thirsty, being dry of mouth, and drank much. Thought she had diabetes! No constipation, but felt somewhat indisposed, having no appetite; slight loss of weight. Suffered from headache and was a little sensitive. — Hypochylia gastrica was established at the provincial hospital. She got worse and came to the Clinic in Febr. 1952 as a depressive psychosis. One finds the picture of a frustration depression with psychic and motor-frustration, depressive thinking, feelings of inferiority, hypochondric ideas. Thought she had a tumor cerebri on account of her headache and because she felt so queer. Was only longing to die. Also anaesthesia dolorosa. Trouble with her sleep of the above-mentioned type. No obsessive symptoms, nor disintegration, nor hallucinations. As the pat. was a little lachrymose, she was first treated with histamine, 1 1/2 mg × 4, for a fortnight and then with Suxil, but not getting well, she was given 4 shocks with good effect. The pat. left the Clinic on 8 June. After a minor gynecological operation, evulsio polypi, her complete health was ascertained at the Clinic in the middle of June. The syntonic personality is obvious. No depression. Sleep and appetite good. — A slight depression returned in late summer lasting 2–3 weeks.

Post-exam. by correspondence in Jan. 1953 revealed good health. Active and alert, weight constant. Did not have the usual autumn depression this last year.

Case 18. 394/53. age 45. Wife of an agricultural worker, 2 children, dead.

Hered. Paternal grandmother and aunt nervous. Aunt committed suicide, had cancer. 5/10 brothers and sisters, healthy.

Somat. Diseases. The pat. had a slight t.b. pulm. dxt. in the winter of 1946–47 and was treated for 2 months at a sanatorium. After that somatically healthy.

Somat. Findings, June 1953: Dysplastic-pyknic type. Height 162 cm, weight 66 kg. Blood-pressure initially 165/100. Cor normal findings. Neurol. examination, nothing noteworthy.

Psych. Premorbid personality. Intellectually normal. Active, straight-forward,

practical. Morning bright. Not labile, nor hysteric. — Since the age of 35 depressed in autumn and spring, having difficulties in managing her household. Syntonic traits.

Case History. No maladjustment during adolescence. Menarche at 14. Menses normal. First child at 19, still-born; 2nd child born some years later, died 4 years old of pneumonia. Pat. married at 23. No marital disturbances. Not frigid. Healthy husband. The family adopted a foster daughter, healthy, and now married. — A few slight depressive periods before she got tuberculosis in 1946. She came to the Clinic first in June 1947 on account of a rather severe depression, having an obvious diurnal rhythm, difficulties in sleeping and anxiety in the small hours, constipation, dryness of mouth and soreness of eyes. Depressed, weary, felt inferior and revealed anaesthesia dolorosa. — Treated policlinically for repeated depressions in Oct. 1947, Sept. 1950, autumn and spring of 1951, and finally in the spring of 1952. On one earlier occasion there was a conflict with her foster-daughter, who was in her teens. Now good relationship. — During her depressions, loss of appetite and of weight (about 3 kg) and occasionally abdominal discomfort with rumbling and distention an hour or two after meals, and before noon. The pat. generally also had angor and pressure on her chest at the beginning and end of her depressions, and a transient rise of blood-pressure up to 180/105. This used to be 160/100 during her healthy periods.

The clinical picture during this time, starting in March 1953 and requiring hospitalization in June 16–26, was of the usual frustration type having the above symptoms. She passed through this period of angor, and was sent home relatively healthy. — Menses always normal, but a certain climacteric picture is found besides that of a depression.

Post-examination, Dec. 1953: Subjectively quite well. No depressive symptoms. Sleep and appetite good. Weight constant. She is a different woman from that of her depressive conditions.

Case 19. 397/53, age 39. Wife of building-worker, 3 children.

Hered. Father, a periodic drinker of middle age. Mother corpulent, died after cholecystectomy when the patient was 4 yrs old. — 5/6 brothers and sisters, one sister having had a period of depression at the age of 35.

Somat. Diseases. Healthy but somewhat obese since the age of 20–25.

Somat. Findings, June 1953: Pyknic type. Height 160 cm., weight 100 kg — usually 90–95 kg. Adiposity, female localization of no special type. Firm in the flesh, youthful appearance. Cor 0. Blood-pressure 150/95. Hypochylia gastrica on arrival at hospital as on previous acceptance. Normal gastric acidity when sent home the first time. An X-ray of the columna vertebralis indicates an anomaly of a vertebra and a slight disk degeneration.

Psych. Premorbid personality. Intellect normal. Social, enjoys work. Morning-active. Contacts and agrees with people easily. Slightly emotional during puberty, and occasionally still assumes unnecessary responsibility. Predominantly syntonic. — Since the age of 30–35 tired, uneasy and despondent during autumn and spring.

Case History. Unhappy childhood on account of her father's alcoholism and a mean step-mother. Menarche at 13. Menses normal. Accepted as a house-maid in a missionary family. Religiously inclined, but never experienced any religious crisis, and has never been a brooding type. Married at 21. Husband also religious, severely ill since 1948 with t.b. pulm. amb. and diabetes, with slight chance of recovery. During 1952 she had "sexual problems" for the first time. Not frigid. Her first depression of a frustration type appeared *before* her husband's loss of health, occurring during autumn and spring. His further decline was simultaneous with an increase in her depression. The pat. was nursed in a psychiatric ward, in May and the beginning of June, 1952, for a depression of an endogenous type.

She suffered from inferiority complexes, having "no right to be happy" and believing that nobody understood her. — "Everything hopeless in the morning." Incapacity for sleeping, and morning-anxiety. Dry of mouth and sore of eyes, and temporary hypochylia (see above). Recovered after histamine treatment.

A slight depression in the autumn, treated policlinically, preceded the actual depression, which began in April 1953. The clinical picture was similar to that of the spring of 1952, but she also had symptoms of depersonalization and giddiness, complaining of headaches and pressure on the chest. Endogenous diurnal rhythm, symptoms from the mucous membranes and a dominating inhibition as earlier. Good reaction on histamine treatment. Among other treatments, the secondary neurotization was dealt with by means of a modified sleeping-cure, and she was put on a diet of calories on account of her adiposity. Sent home, healthy.

On post-examination in Dec. the patient was quite well, weight constant, sleep good. Some anxiety in the autumn when her husband was brought home from the sanatorium, and had an attack of haemoptysis again.

The exogenic factors of this case should be noted: besides a psychotrauma in childhood there is predominantly the actual psychic stress of her husbands's illness.

Case 20. 547/53, age 26. Wife of a civil engineer, one child.

Hered. Her mother made an attempt at suicide at the age of 30 in connection with a broken engagement. 2/2 sisters.

Somat. Diseases. Healthy. Neither anaemic nor sensitive to infections.

Somat. Findings, Aug. 1953: Undecided type. Height 175 cm, weight 65 kg. Blood-pressure 130/90. Neurology: normal findings.

Psych. Intellectually normal. When healthy she was socially inclined. Gets along with others. Even and normal working capacity. "Not hysteric." No conflicts. No periods of insufficiency, but is generally tired in the spring. Always a little emotional.

Case History. External milieu suitable since childhood. Emotional as a child. Restless sleep, and faddy about food during a period. No biting of nails, nor bedwetting, and showed no maladjustments during her teens. Was a good-natured child. Menarche at 13, menses normal. Not frigid. Married at 24. First child at 25 in the spring of 1952, a healthy daughter. Weary and slightly depressed during period of nursing. Change of environment and an increased burden of work owing to her husband's removal to another community in May 1953. Being tired in the spring she felt her incapacity for work more than otherwise. A pronounced degeneration in June with loss of appetite and weight, depressive delusions accompanied by total incapacity for work. Experienced a lack of emotional contact with her family. Had no feelings for her husband and child as before. A vague attempt at suicide by drowning (Aug.) as well as infanticidal intentions resulted in her acceptance at the Clinic. Revealed psycho-motor frustrations of a certain degree, having depressive delusions. The pat.'s morbid state verged for a short time upon *Beziehungswahn,* but there was no rigidness, nor disintegration, nor incoherence, indicating no negativism nor autism.

The predominating symptom was, however, her anaesthesia dolorosa, her great sorrow for not having feelings for her husband and child. She believed she was a bad mother, and her vague broodings on infanticide were entirely inspired by altruistic motives, in order to save her child from living in "this miserable world". An obvious diurnal rhythm was ascertained, but she did not suffer from any severe anguish while staying at the clinic. She gradually recovered from her depression, being treated with opium, psychotherapy, and insulin before it was necessary to administer any shocks. Was sent home in good health on Sept. 23.

Post-examination, Dec. 1953: The pat. is subjectively well. New will to live and fresh confidence. Her sleep good, as well as her appetite. Increased somewhat

in weight. Is once more able to feel for her family. Her libido returned, which was absent during her depression. Accessible, the syntonic traits being confirmed.

Case 21. 271/53, age 46. Wife of a foreman. No children.

Hered. Father stingy, rough, and somewhat hot-tempered. On the whole healthy till his death. Her mother probably had asthma. One brother had diabetes mellitus. An aunt was for a time nursed at a mental hospital. A maternal cousin and her children were insane, and finally an uncle of her mother's committed suicide by drowning himself. 1/5 brothers and sisters.

Somat. Diseases. On the whole healthy, was never treated at a hospital.

Somat. Findings, April 1953: Dysplastic type, rather heavily built. Height 156 cm, weight 56.1 kg. Her flesh was normal. Cor 0. Blood-pressure 140/90. Somatology and neurology: normal findings.

Psych. Intellectually not below the level. As to her disposition, she was always somewhat emotional. Particular without being pedantic. Practical, likes domestic work, needlework etc. Usually morning active. Gets her housework done in good time. She is sociable, being a member of sewing circles, but does not always take the first step in making acquaintances. No hysterical traits. Usually she is despondent and anxious in the autumn, being then without initiative: "I can't get anything done! Everything piles up on me."

Case History. No maladjustments as a child. Developed late. Menarche as late as the age of 17, after which her menses ceased for 3 months, but since that it has always been regular. Coitus at 20, married at 34. Sex. not frigid. No children; involuntary sterility. Menopause at 44. Her marriage is, under the circumstances, happy, she and her husband being mutually attached. The pat. had her first period of depression one autumn during her late teens. She was nervous, anxious, and despondent, and had to see a doctor.—A second period of depression came in the autumn of 1945 when she was 39 years old. The pat. became despondent, nervous and anxious, waking up in the small hours in anguish. (On this occasion a somewhat too high basal metabolism was found [+ 20 per cent!]. Her thyroid glands were policlinically given a few X-ray treatments.) She had recovered by the following spring.

The depression of chief interest came in Dec. 1952, released in connection with her mother's death, which the pat. experienced as a shock. Her mother died of an acute cerebral haemorrhage, and the pat. was the one who found the deceased. This caused an acute depression, she began brooding, being beset with self-reproach and anguish, partly as angor (but without palpitations). She had difficulties in sleeping, a typical endogenous diurnal rhythm, the mornings being bad. She lost her appetite, was thirsty, and drank much coffee—also to keep going; was dry of mouth and eyes and could not weep. She lost about 10 kg in 4 months. She harboured suicidal intentions. On the morning of April 16 she took the train to go to her mother's grave, intending later to disappear after leaving a farewell letter to her husband. She got on the wrong train and came to her relatives, who arranged for her to be taken to the Clinic. On account of the typical clinical picture and the anamnesis, she was supposed to have an endogenous depression, mainly of an inhibition type, and was given ECT. The pat. recovered very fast after 3 el-shocks, put on weight, and said her feelings and experiences began to be the same as when she was healthy. Her sleep and her will to live returned. Was discharged in rather good health on May 29th.

Post-examination in Jan., 1954: The pat. claimed that she was not fully restored until a month or two after her discharge and after her summer holidays. She remembered her illness well and her suicidal thoughts. The syntonic trait of her constitution was confirmed. She was sociable, accessible, and not particularly forgetful. She did not seem to be below the level. She could manage her domestic duties, was not hesitative, and felt rather confident in herself.

Case 22. 61/53, age 52. Wife of a building-worker. 5 children.

Hered. Father labile and somewhat nervous. Mother healthy. 5/6 brothers and sisters, apart from 2 or 3 brothers and sisters, who died as infants.

Somat. Diseases. On the whole somatically healthy.

Somat. Findings in Jan., 1953: Pyknic type. Height 158 cm. Weight 63 kg. Cor 0, blood-pressure 155/85. ECG, moderate sinus tachycardia and S–T depressions of a coronary type. No signs of incompensation. Moreover, somat. and neurologically nil.

Psych. Premorbid personality. Intellectually normal. The patient was industrious and efficient. Found it always easy to contact others. Emotional and sympathetic. Somewhat sensitive and easily offended. Found it easy to work and accomplish her duties. Has taken active part in congregational work, been the leader of a sewing circle, etc. Not easily flurried. Manifested obvious syntonic traits.

Case History. At the age of 14 she lost her father, who was a tenement soldier. The mother cared for the children, some of whom had then grown up. No maladjustment during childhood, no crises in puberty. Married at the age of 20. Five children healthy, born between 1921 and 1942. Fertile period between the age of 13–50. No gynecological disturbances. Religiously inclined. Harmony in marriage. Husband healthy; economy satisfactory. First period of depression in 1936 in connection with a delivery and the death of her mother. She grew depressive, anxious, had attacks of anguish, and partly also of weeping. Not completely restored until after 2 years. Was treated at a cottage hospital for 7 weeks and was given sedatives. In the autumn of 1949 there was again a period of depression with morning anguish, weariness and even at this time attacks of weeping. In the summer of 1951 their house was repaired, and the patient had much extra work to do and little sleep (menopause in Jan., 1951). Weary and depressed during the autumn. Consulted a psychiatrist in Jan., 1952, among other complaints for poor sleep since Christmas. Made an attempt at suicide by means of soporifics on Febr. 7th, and was brought to the Psychiatric Clinic in February, 1952. When explored psychically, she stated that since Christmas she had suffered from dryness of mouth and constipation, despondency, brooding, pain in the neck for a rather long time, and painful palpitations of the heart. No definite endogenous rhythm of late. She was tormented by the fact that she was unable to take care of her home. Her malady was interpreted as an endogenous depression. An abvious improvement after ECT (5 shocks). Discharged in the beginning of March, 1952. Admitted the second time during April to May of the same year—this time with a more pronounced diurnal rhythm, but not so frustrated and full of anguish as on her first admittance. She was treated with histamine and 2 el-shocks, giving a certain positive effect. Admitted again in August, she revealed approximately the same picture; she brooded over her incapacity for work, but no longer harboured any thoughts of suicide. After a sedative treatment with insulin without any obvious effect, the depression diminished after ECT (3 shocks). Sent home in good condition at the end of August.

She was fully vital, able to work and to take care of her home as before until just before the Christmas of 1952. The depression of main interest began at this time. She grew depressed and enfeebled, being unable to carry out the common duties of her home. At this time she manifested a pronounced diurnal rhythm with increased disturbances during the mornings, but was also tired and uneasy in the evenings. She had vague delusions of sin, incapacity for sleep, and anguish in the small hours. Her husband claimed that she never got started until in the afternoons. When she was admitted into the clinic in Jan., 1953, her picture was that of an inhibition depression; she was at the same time anxious and afraid of becoming insane and in other respects showed the same picture as on earlier occasions of illness. Possibly appeared somewhat dull of mind on certain occasions. After 5 el-shocks with narcosis she was definitely discharged from the

Clinic in the middle of May, 1953, as being improved. She had increased in weight, her depression being mitigated, but on certain days she still felt uneasy. Her sleep was not fully satisfactory, and her eagerness for work had not returned.

At the post-examination in March 1954 the patient stated that she had not quite recovered until then. Her sleep had now returned and also her appetite. Her will to live was renewed. The syntonic trait of her constitution was confirmed. She was pliable and well-disposed, and did not appear to be "below the level"; and there were no indications of any psychical rigidness or dullness.

Case 23. 649/51, age 36. Wife of chauffeur, 2 children.

Hered. Her father died from heart disease, mother living, being rheumatic. 5/5 brothers and sisters. One brother committed suicide when between 20–30 years of age. One brother was treated in a mental hospital for schizophrenia.

Somat. Diseases. Healthy, with the exception that she was operated on for gall-stone in 1951. No lengthy anamnesis, no jaundice, no complications. No noteworthy gastro-intestinal troubles before or later.

Somat. Findings in June, 1953: Undecided type. Height 166 cm, weight 94 kg. Adiposity of female type, firm flesh. Cor 0, blood-pressure 150/90. Scar on abdomen after operation for gall-stone. Other somat.-neurological findings: nil.

Psych. Intellect normal. When healthy, she is cheerful, vital, and industrious. Morning-active. Extrovert. She finds it easy to win friends and likes company. Is not much affected by adversity and knows how to put difficulties aside. Orderly, but not pedantic. Musical. Possibly somewhat moody during spring-time in maturity.

Case History. Parental home good, childhood happy, she developed normally; no maladjustments as a child, nor during puberty. Menarche at 12–13 years of age, no gynecological complications. Not frigid. Harmony in marriage. Husband healthy as are her two children, aged 12 and 8 years. Economy satisfactory. Is happy in her home which she manages easily when she is well. She has also occasionally had extra work at the telephone exchange when her children grew older. Is religiously inclined, just as her parents, and both husband and wife belong to the Swedish Mission Covenant. Has had no religious crisis, never brooded on religious matters. Her first period of depression occurred in a mild form at about the age of 17. A certain despondency and a general feeling of discomfort was noticeable, but no serious symptoms. She became well after a month or two. Next period came in the spring of 1946, when she was melancholy and depressed. Even this period was very mild and brief. The third period of depression in the autumn of 1947 necessitated her being treated at the Psychiatric Clinic. Her picture was that of a slight frustration depression; she felt "awfully tired", being worse in the mornings (occasional morning-anguish); had to force herself to work; initially dry of mouth, lost appetite and weight. She was at the same time anxious and uneasy, occasional feelings of anguish in her chest. A very good effect with ECT (2 shocks). Strong and healthy, and with an apparent rise of her spirits. Was discharged as healthy in the beginning of Dec. 1947. Her fourth period of depression began in March and April 1951. The pat. revealed the same picture as in 1947. Simultaneously she had a gall-bladder attack, and when her depression increased she received ECT, 3 shocks (policlinically) in the months of May and June, 1951, with a temporary improvement as a result. Was operated on for gall-stone on July 1st, without complications. During convalescence she slipped back into her depression, grew tired, frustrated, felt dry in the mouth, was sad, but could no longer cry. Revealed an anaesthesia dolorosa, had not the feelings she wanted for her children, nor for her husband. Became frigid. Her condition grew worse and the pat. was admitted into the Clinic in Oct. 1951. She did not manifest a very severe frustration depression. Her anguish was not predominant; there were no severe symptoms. Good reaction

after 3 el-shocks. Her depression was interpreted as a released endogenous depression after her operation in the summer and as provoked by a relatively great burden of work. She was discharged in good condition in Nov. 1951.

She kept well until the month of May 1953 when she had her *fifth depression,* this time without any obvious cause. Remained in bed during most of the forenoon, not being able to manage her duties at home. She was restless, having an endogenous rhythm of sleep with difficulties in sleeping in the small hours of the morning, and anguish. On clinical examination in June an obvious psychomotor inhibition was observed, and she manifested endogenous symptoms of a diurnal rhythm and, as before, dryness of mouth. On the other hand, no gastrointestinal disturbances were noticed. No schizophrenic symptoms. No disintegration nor splitting, nor obsessive symptoms. Obvious improvement after 3 shocks. She slipped back, however, into her depression during the summer and applied for admittance into the Clinic in September as being not fully recovered. She again received 3 shocks, and was discharged in good condition in October 1953.

Post-examination in March 1954: Pat. sociable, showing syntonic traits. She was not below the level nor dull; gentle and pliable. Memory and capacity for concentration good. She was happy and optimistic, sleep and appetite good. Was able to work at the telephone exchange.

Case 24. 130/53, age 56. Wife of farmer, 6 children.

Hered. Father died of cancer ventriculi, 48 years old. Grandmother, suicide during depression, 50–60 years old. Mother living, 87 years old, healthy. 2/3 brothers and sisters, of good health.

Somat. Diseases. Always in good health. On X-ray examination of the lungs there was accidentally found, in the first right intercostal space, a density partially calcified and as big as a small chestnut, as well as some fibrosis between the former and the right hilum (with a minute amount of pleural affusion, temporary after shock). Nothing of actual interest.

Somat. Findings, Febr. 1953: Pyknic type. Height 162 cm, weight 58 kg. Cor 0. Blood-pressure 140/95. Neurology: nothing noteworthy.

Psych. Premorbid personality. Intellectually normal. Industrious, extrovert, "the pillar of the house". Not labile nor irritable. No hysterical manifestations. Sensitive. Generally tired in spring during maturity, having restless sleep and difficulty in getting started in the mornings. Pat. is a syntone.

Case History. Parents' home good; no maladjustment during adolescence. Fertile period 14–53. Married at 20. Six partus, 2 children died as infants, 4 living, healthy. No gynecol. disturbances. Sex life: no remark. Not frigid, coitus still twice a month. Husband, a farmer, has had heart trouble. Pat. had a mild depression earlier, in spring, rather severe in 1951. Morning anguish and "brooding on unnecessary things". At the same time, slight and temporary anaemia. Took iron regularly for 2 years, except for short periods. New spring depression of the same type in March 1952 with a spontaneous remission in summer. Lingering depression from before Xmas, 1952, but she could execute her duties. Degeneration in Febr. 1953, with melancholia of the previous type, "everything meaningless". Frustration depression: "Wants to work, but cannot get started." Morning anguish. Difficulties in sleeping towards 3 a.m. Dry of mouth in the mornings. "Cannot weep. No tears." Self-reproach and inferiority complex. No delusions of sin, but had the conviction of being incurable. Pat. left the Clinic on Febr. 24, after a certain improvement, at her own risk and that of her family. Raptus melancholicus at 3 a.m. on 11 April. Wanted to blast herself with dynamite, having lighted a fuse and also started a fire. Lost 3 kg since taken to hospital in Febr. Now 53 kg. General psychic degeneracy with anguish at night, apathy and depressed brooding. On examination on 11 April dominant frustration depression, frustration of thought, a certain anaesthesia dolorosa, and obvious motor frustra-

tion. No disintegration, nor hallucinosis. El-shock treatment on Apr. 16–28. After 5 shocks quite healthy. Sent home on Apr. 30, after 9 days of sedative insulin therapy (max. 32 units).

Post-examination in Dec. 1953: Pat. and her husband claim good health since return home and ability of working as previously. Appetite and sleep good. Put on weight somewhat. Now 60 kg. No anxiety nor anguish. No psycho-motor frustration. Pat. is syntonic, and emotionally soft and well-disposed, seems to be on a normal level.

Diagnoses of Certain Other Depressive Conditions of a Mixed Type

Table 27 B.

Diagnoses of patients having higher values when discharged than on their arrival at the hospital.

Three men and 13 women.

Psychasthenia gravis. Born 1914.
Depression of a primarily chronic type with atypical traits. Born 1894.
Asthenic insufficiency (hysterical traits). Born 1915.
Reactive insufficiency, "overworked". Born 1896.
Insufficientia et depressio mentis praesenilis. Born 1901 (paranoid traits).
Post-puerperal schizophrenia (depressio mentis). Born 1924.
Presenile depression (rigidity and poor therapeutical results). Born 1887.
Psychopathia (alteration of personality, suspected schizophrenia). Born 1923.
Depression, psychasth. and praesenium. Born 1894. To mental hosp., unimproved.
Psychasth. Born 1928.
Depression, psychasth. (psycho-infantilism). Born 1926.
Psychopathia, depressio mentis. Born 1926.
Depressio mentis (post-puerperal asthenia). Born 1923.
Presenile insufficiency. Born 1889.
Involutional depression (abusus ethylicus). Born 1900.
Depressio mentis praesenilis (pre-eminently dysphoric). Born 1900.

Table 28 B.

Diagnoses of patients having a higher serum-iron value in the evening (inverted curve). Two men and 13 women.

Reactive insufficiency. Asthenic and hysteric traits. Born 1912.
Reactive insufficiency. Born 1917.
Involutional depression with asthenic traits. Born 1906.
Obsessive compulsive neurosis, schizoid traits. Born 1925.
Endogenous depression with schizoid traits. (Acrocyanosis.) Born 1920.
Endogenous depression with "Beziehungswahn". Born 1927.
Asthenic insufficiency, depressive traits. Born 1916.
Depressive condition with paranoid traits. Born 1906.
Depression with asthenic traits. Born 1921.
Involutional depression with pronounced psychasthenia. Born 1894.
Depression with psychasthenia. Born 1928.
Endogenous depression. Hysteric traits. Psycho-infantilism. Born 1926.
Depression. Psychopathia. Born 1926.
Post-puerperal depression. Psychasthenia. Born 1923.
Depression and presenile insufficiency. Born 1900.

Summary

In *Chapter I* a definition of concepts has been undertaken. The conventional classification into such cases as reçover, e.g. manic-depressive psychoses, and such as become more or less stamped by their malady, e.g. schizophrenia, is confirmed. There is further a discussion on symptomatology, the importance of constitution, heredity, and releasing factors. Stress is laid on the difficulty of making a correct diagnosis in certain borderline cases, and on the importance of prognostic investigations. Current discussion on psychoanalysis in depressive conditions is briefly touched upon. There then follows an account of scientific and medical therapy, in which ECT at present predominates in the treatment of conditions of so-called endogenous depression—a clinical concept which is further developed.

In *Chapter II* the problem is presented concerning iron and its importance in the metabolism of cells, which is believed to be reduced, or changed in some way, in endogenous depressions.

The distribution and metabolism of iron in the body are reviewed in *Chapter III*. The author stresses the changing distribution of iron at different ages of the individual, both tissue iron and serum iron. The relative abundance of iron in the central nervous system is emphasized. Definitions are given of tissue iron, serum iron, and the iron-binding capacity of serum (transferrin). Finally, a few clinical viewpoints on serum iron and transferrin and their mutual relationship are mentioned.

Chapter IV deals with earlier investigations into the iron metabolism and red-blood picture in mental illness. A record is given of the increase in tissue iron of the basal ganglia in various types of psychoses, a lower spinal-fluid iron and serum iron occurring in acute states of schizophrenia. The influence of ECT on the serum-iron level is expounded, as well as the author's earlier investigation into the serum-iron level of endogenous depressions. Research into the red-blood picture of mental disorders did not yield results of major interest.

The methods used are presented in *Chapter V*. That of Heilmeyer and Plötner modified by Vahlquist was considered to be applicable in determining serum iron. The iron-binding globulin was determined by the method of Schade and Caroline, as modified by Rath and Finch; and the plasma volume was estimated by Evans blue-dye method. Use was made of routine clinical haematological methods. Standard statistical methods were applied.

Chapter VI contains a description of electro-shock technique: firstly, the ordinary method of MacPhail-Strauss; and, secondly, the apnoeic-diffusion oxygenation method with total muscular relaxation (Holmdahl), which has been the method of routine at the Clinic since 1953. Since that year a Siemens "Konvulsator III nach v. Braunmühl" has been in use.

An experimental study on rabbits, presented in *Chapter VII*, proves that the serum-iron level is not influenced by ECT to any noticeable degree in normal animals. The same is the case with regard to stress in the form of starvation for 48 hours, which brings about obvious haematological changes. A tendency to an increase in weight was seen in animals treated with shock, compared with the controls.

The differential diagnosis of the main clinical material is discussed in detail in *Chapter VIII*.

Clinical aspects of the cases are developed in *Chapter IX* with regard to the civil and the social status, distribution of age and sex, somatic type, previous physical illnesses, releasing factors, and psychic types. There are data on the first appearance of the depression, the number of preceding depressive periods, the history of the period of main interest and its duration, the clinical picture of this period, treatment and its results, and so on. The main series amounted to 39 patients (15 men and 24 women), the case histories of whom are presented at the end of this book.

My laboratory findings are given in *Chapter X*. A high serum-iron value was found in endogenous depressions, the iron-binding capacity being within normal limits. The high serum-iron value returns to normal on recovery. On treatment with electro-shock the serum iron fell successively to the normal value. A remarkably high iron-binding globulin and a low serum iron were found in depressive conditions of suspected schizophrenia; in these patients there was often a pathological diurnal serum-iron curve, with low morning and higher evening values. Iron-tolerance curves (intravenous injections of ferrous sulphate) were high and sluggish in endogenous depression, in accordance with the high saturation of the iron-binding globulin and the intolerance for iron shown by patients to whom injections were administered.

The current belief that a high morning value for serum iron depends on sufficient and undisturbed sleep proved to be erroneous. The patients often suffering from poor sleep possessed abnormally high serum iron in the mornings. The author stresses the assimilation of food and the function of the liver as factors influencing the serum iron (starvation experiments on man).

Chapter XI presents certain aspects of the question concerning the cause of abnormally high serum iron in endogenous depression, and a changed diurnal serum-iron curve in depressive states of suspected schizophrenia. On the basis of my findings, a few questions are

raised regarding haematopoiesis and the function of the RES. Mention is made of the significance of the sympathetic adreno-cortical system. Finally, allusion is made to the importance of the liver function and its disturbances in mental disorders. The cause of the high serum iron in endogenous depressions is regarded as a complex of unknown changes in the organism.

Chapter XII contains case histories and tables of diagnoses.

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Bo Källström

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